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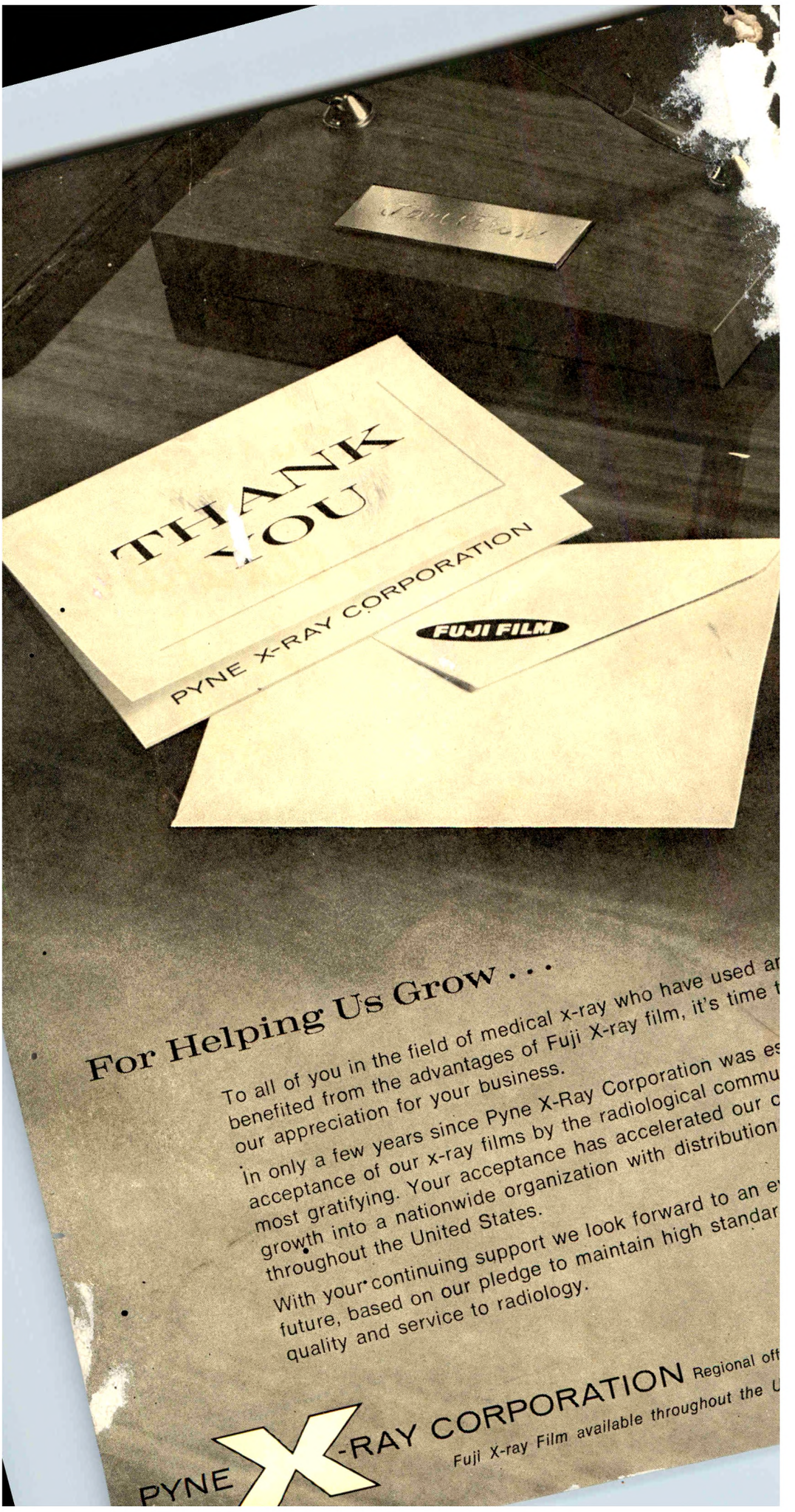
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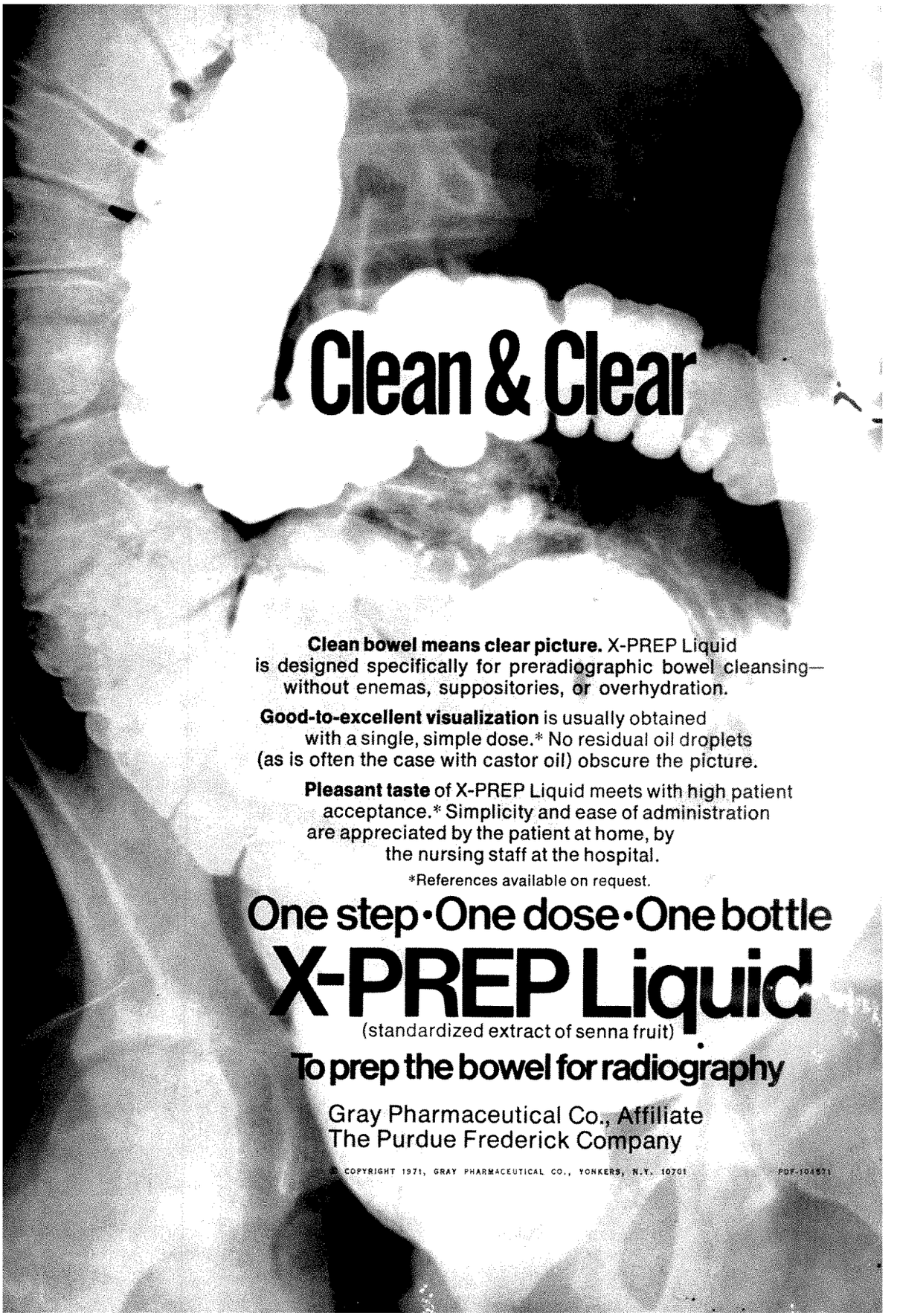
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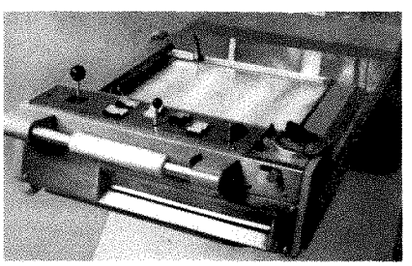
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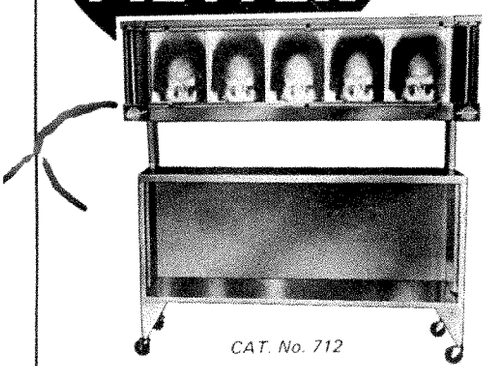
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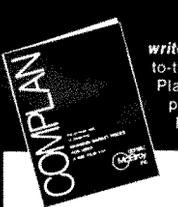
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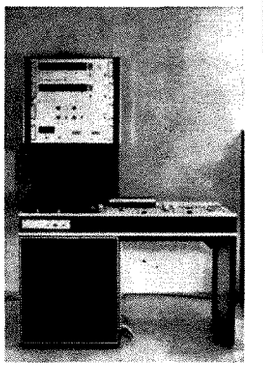
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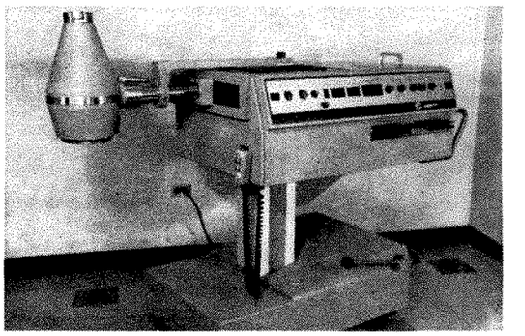
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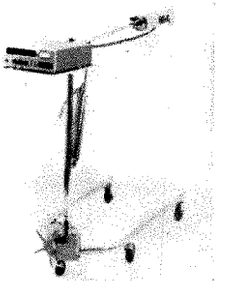
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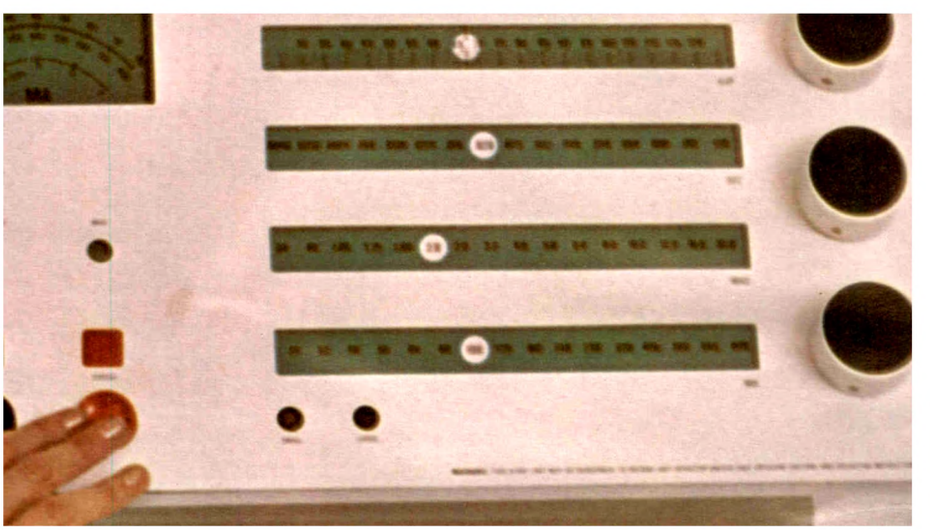
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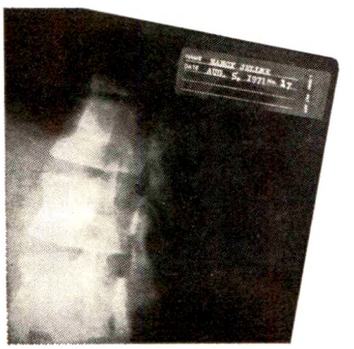
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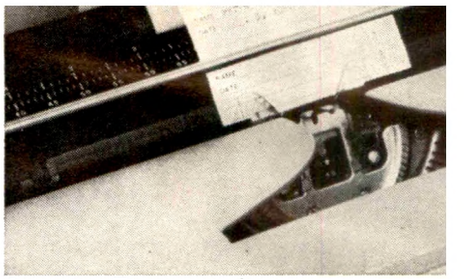
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When it comes to patient-film identification, you can't beat the system.

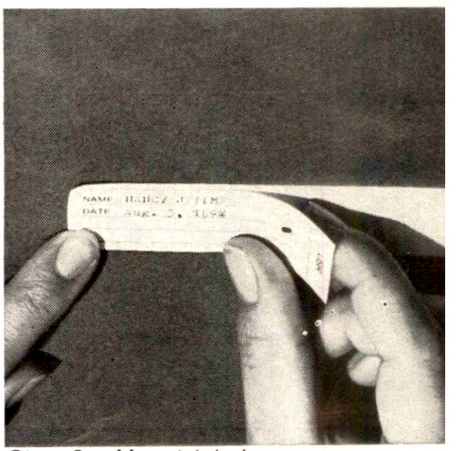


Halsey Chron-I-System. It lets you see the problem in a new light.

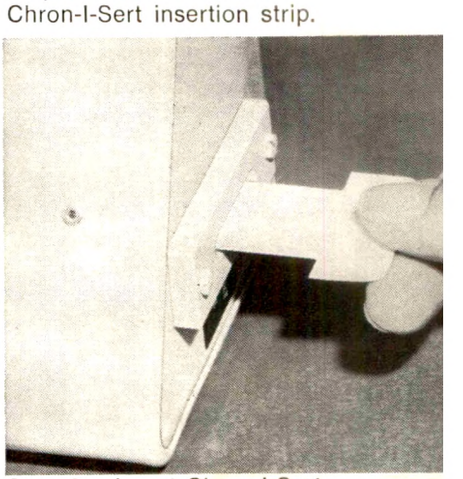
New Halsey Chron-I-System provides positive patient-film identification in ordinary daylight — without opening the cassette or entering the darkroom. Chron-I-System is a simple 4-step technique that takes only seconds. The system consists of special labels, insertion strips, an Exciter and Halsey Chron-I-Settes. It's extremely flexible — can also be used with patient "Charge Plate" imprinters — and permits positive film identification before or after X-ray examination. Chron-I-System requires no X-radiation, thus no "burn-out" or "coning cut off". It eliminates identification printers and minimizes the possibility of film misidentification. Halsey Chron-I-System. You can't beat it for speed or efficiency. Call your dealer for a demonstration today.



Step 1. Type or write patient data on special label.



Step 2. Mount label on Chron-I-Sert insertion strip.



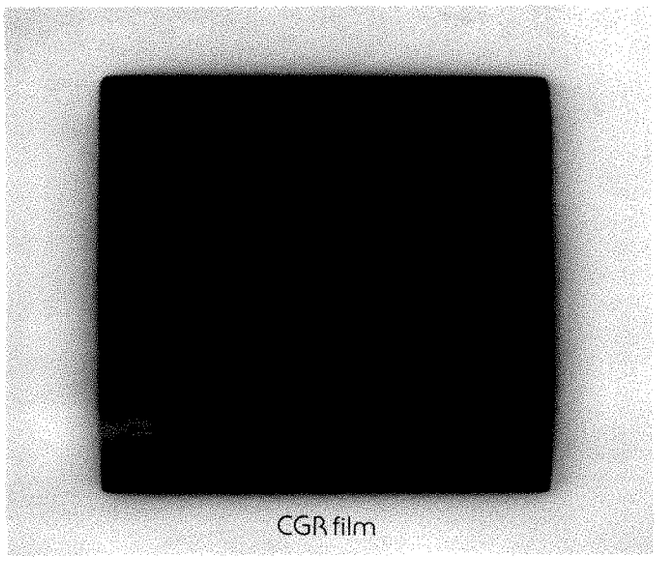
Step 3. Insert Chron-I-Sert into Exciter for a few seconds.



Step 4. Place Chron-I-Sert in Chron-I-Sette slot. Remove in 3 se

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The first beam limiting system that works.

This film was exposed using CGR's new X-ACT beam limiting system. Compare this with typical results from other units. And you can see there's no comparison.

CGR has practically eliminated extraneous and off focal radiation. We've been able to do this because of significant design changes unique to our system. Film quality is exceptional.

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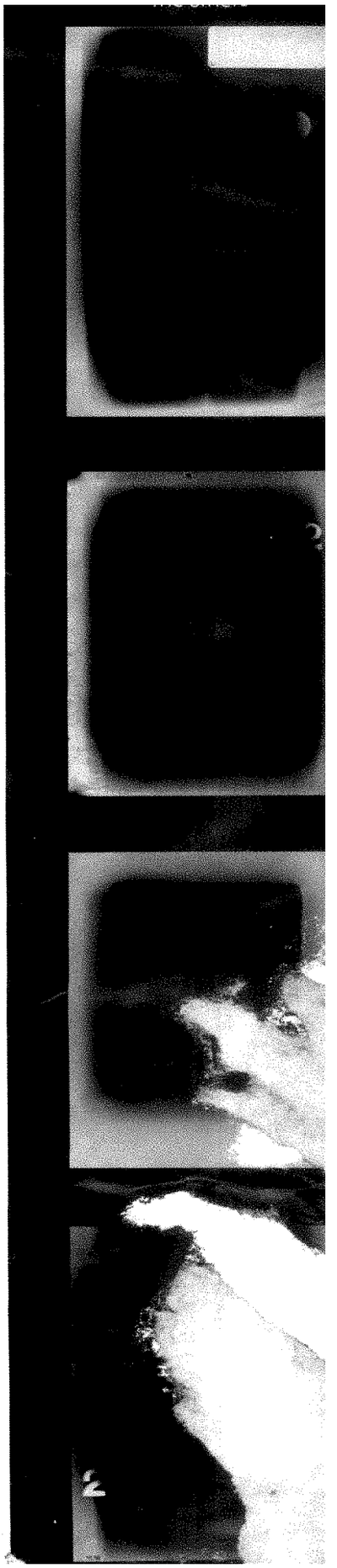
Field illumination light is feather-touch controlled. Light and x-ray field areas are absolutely synchronized. A reliable solid state timer is integral and automatically terminates light at the end of 50 seconds. And its lamp is long life, high intensity, iodized quartz.

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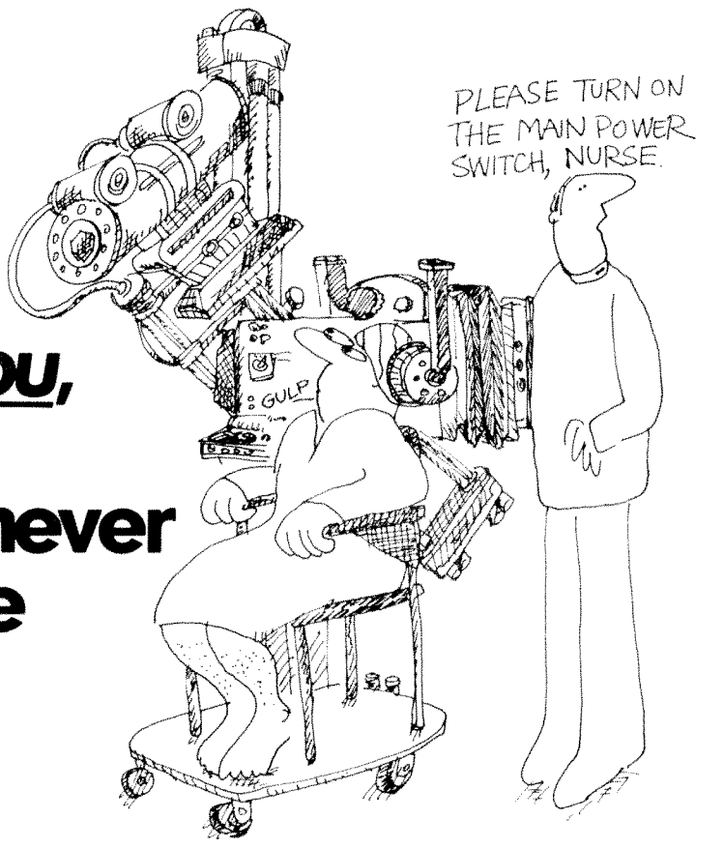
X-ACT meets and even exceeds HEW standards.

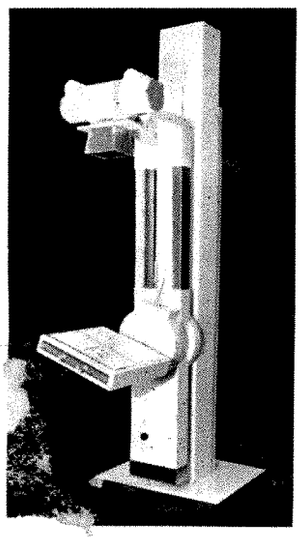
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It may not bother *you*, but the patient's never seen one before.



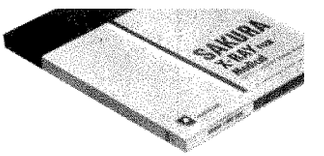


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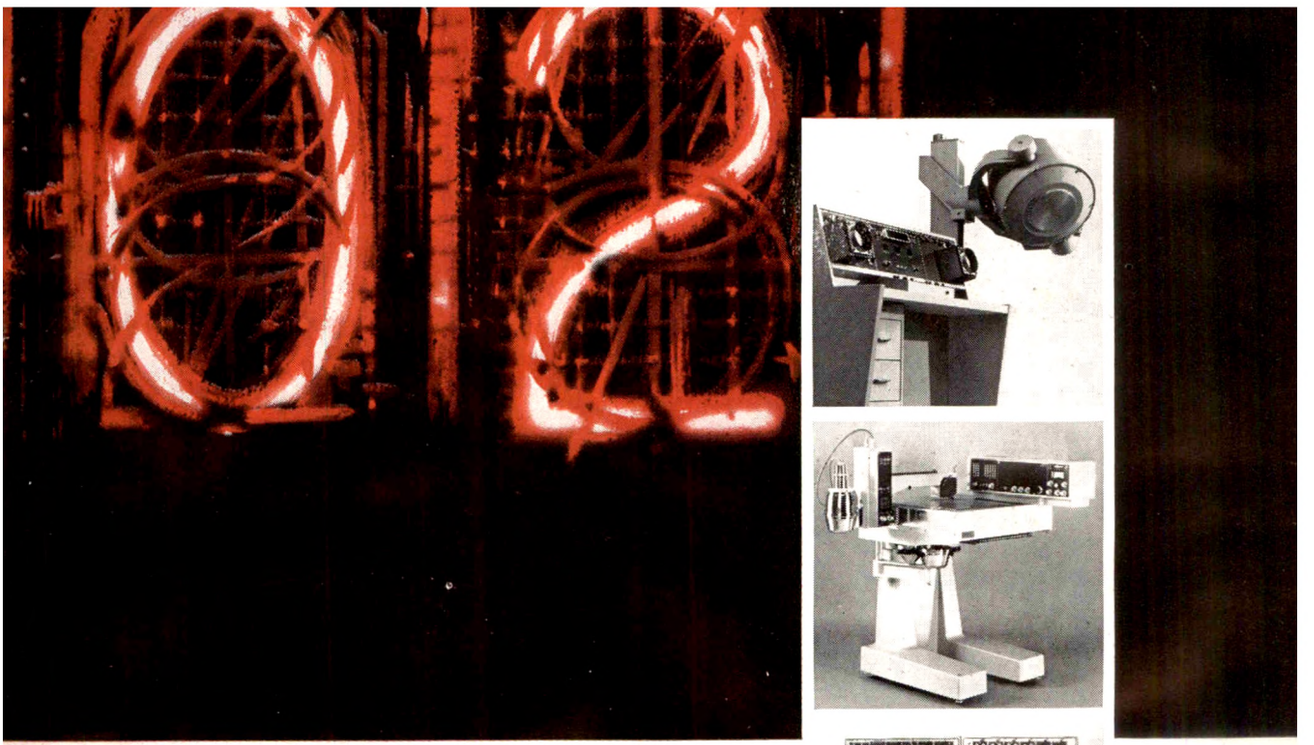
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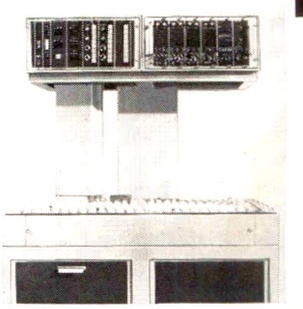


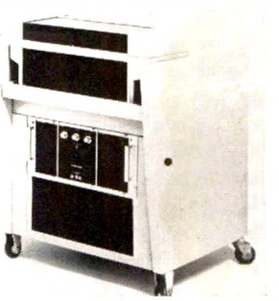


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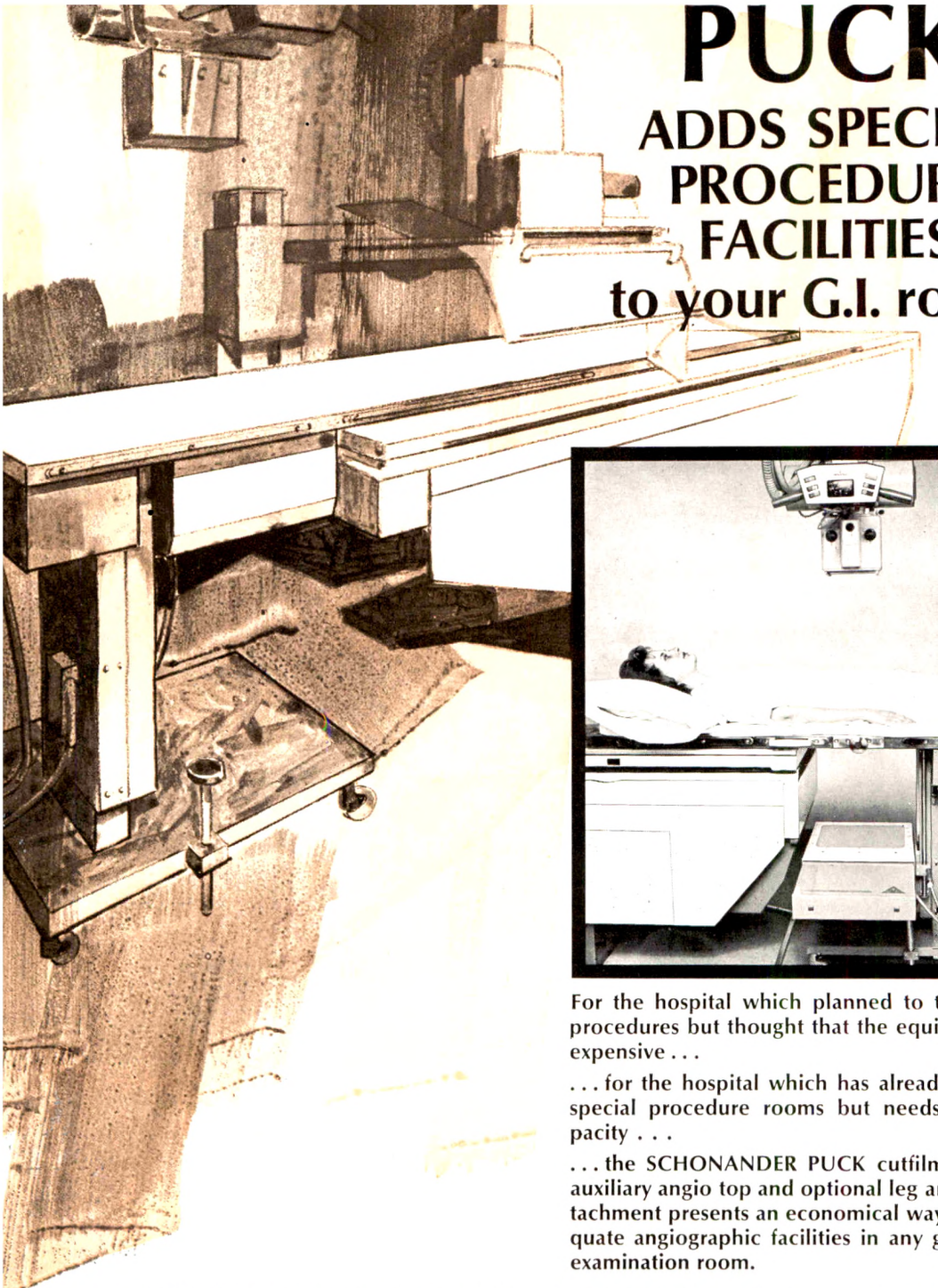
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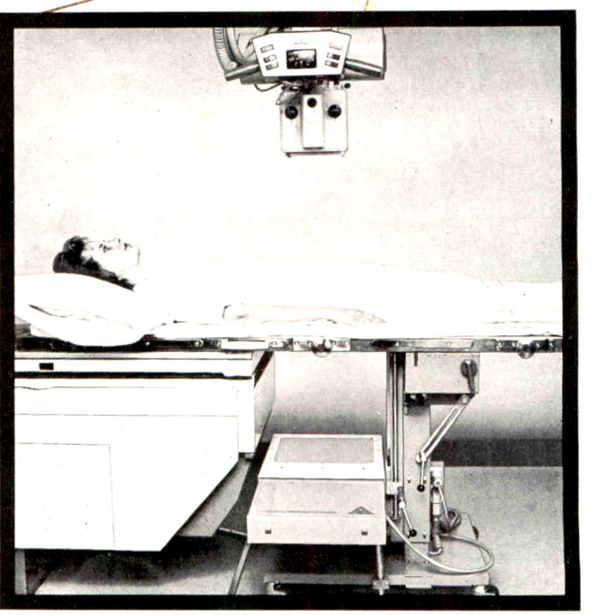
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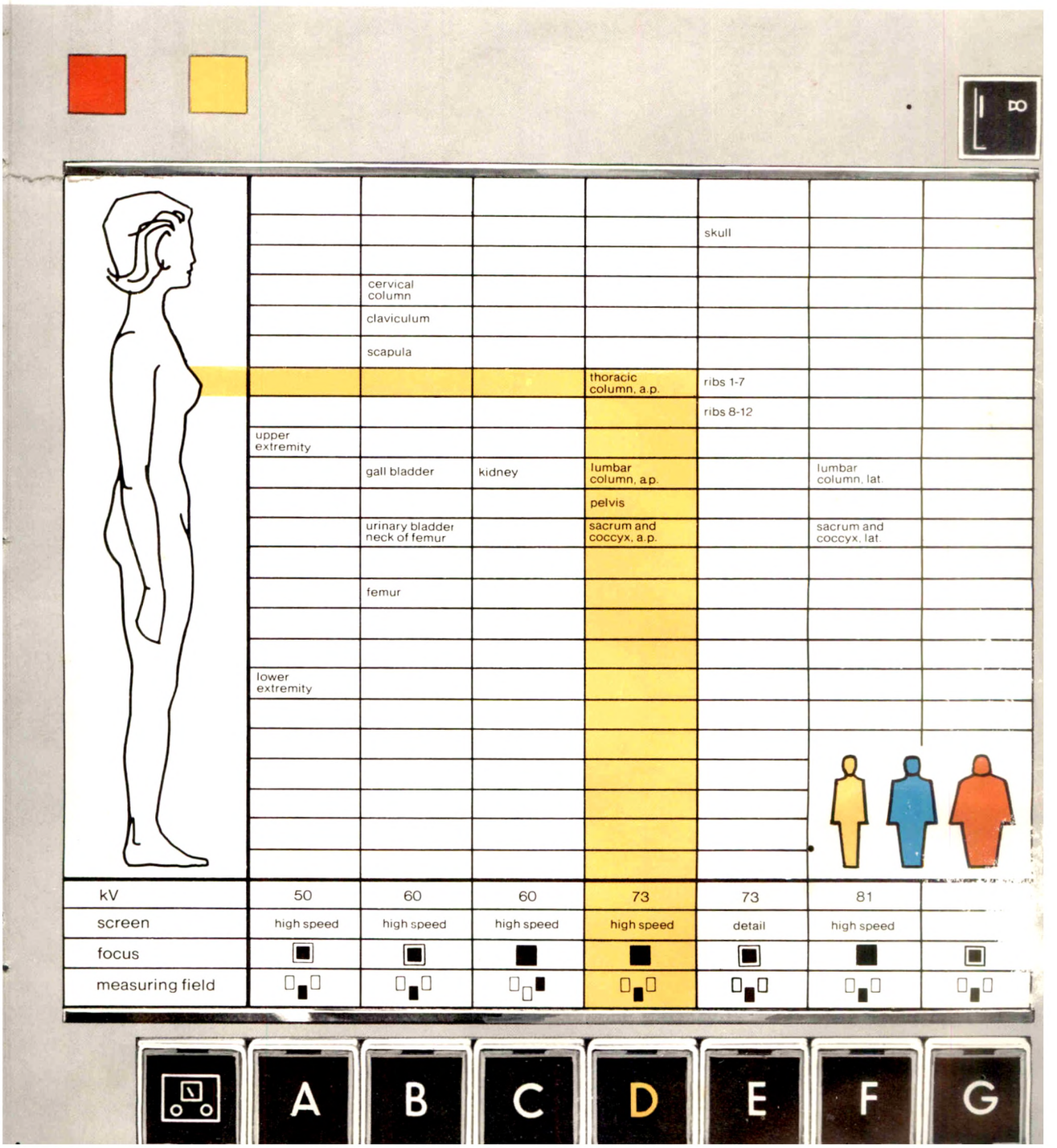
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Siemens presents a systems-approach to radiology.



Siemens Tridoros Optimatic.
A multi-unit system with individual local unit consoles.



Siemens now offers a way to expand radiological facilities while at the same time optimizing the use of equipment and key personnel.

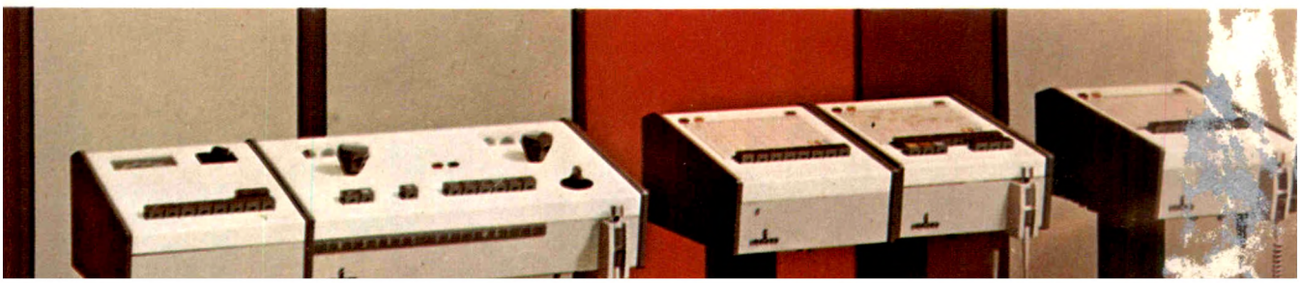
The Tridoros Optimatic system consists of a single centrally located, time-shared master generator with an analog computer and three or more pushbutton operated local consoles.

A new Tridoros Optimatic installation with four examination units usually costs considerably less than a similar setup using individual generators. But the major advantage of the new system is in the way it cuts to a minimum the number of decisions and adjustments the operator has to make to get optimum results.

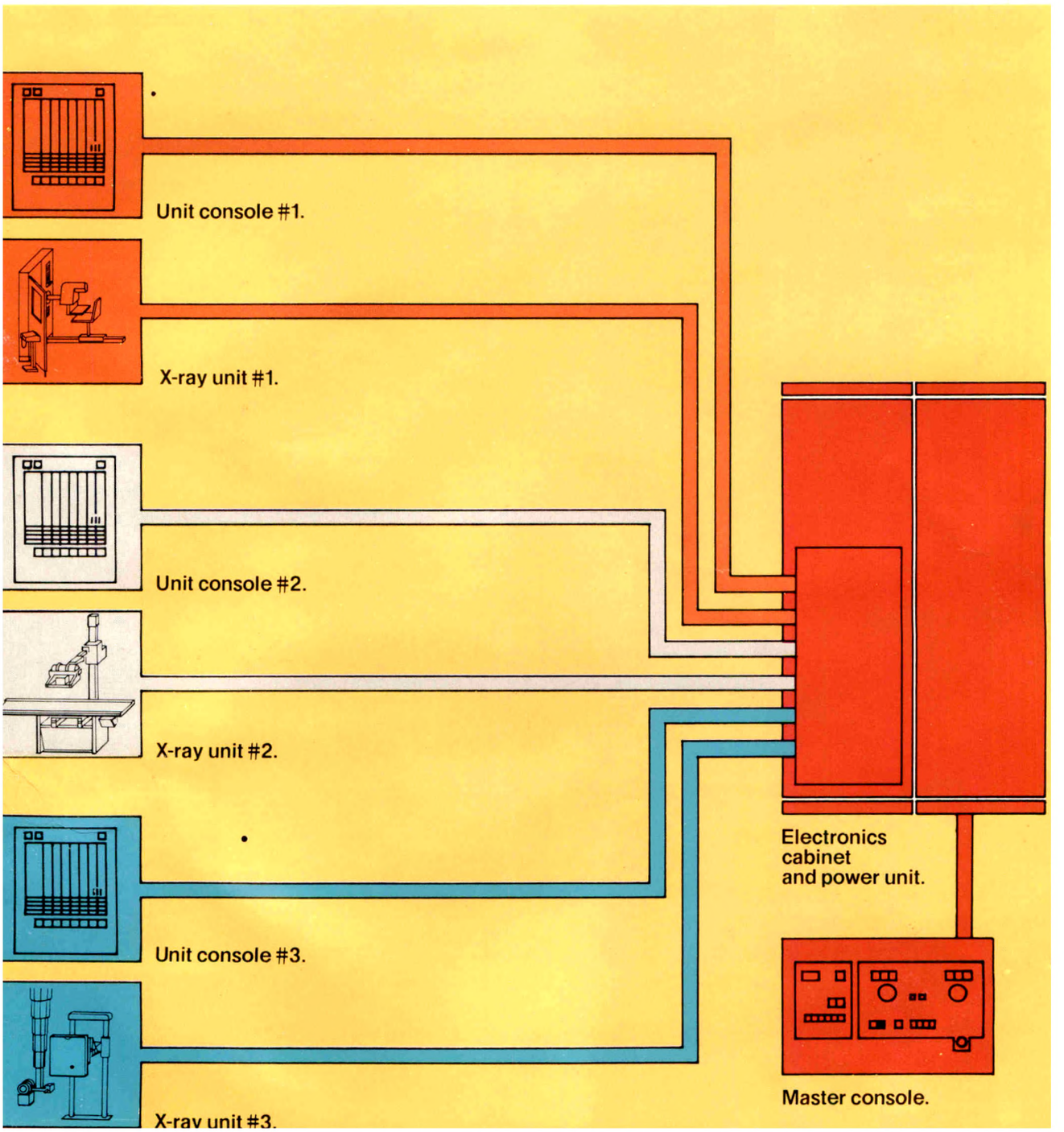
Technicians can now handle a much greater patient load while producing consistently superior radiographs.

At left: Technician starts automatically timed exposure at unit using overtable tube.

Below: Elements of the Tridoros Optimatic system including electronics cabinet (left rear), power unit (right rear) and left to right, master console and three unit consoles.



Consoles are "human-engineered" to provide organ-related pushbutton exposure control.



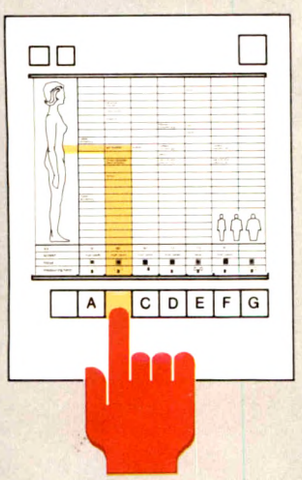
A Tridoros Optimatic unit console is set up in the immediate vicinity of each examination unit so that technicians are close to their patients.

To set the exposure at one of the consoles, the technician pushes one of the seven organ-related buttons. This automatically selects the kV, focal spot, screen combination and film blackening needed for the particular type of exposure to be made.

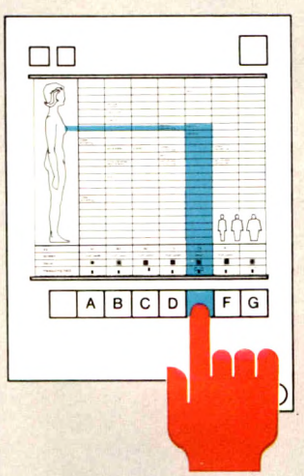
These unit console panels have a number of important advantages. They make data selection simpler than ever before. They greatly reduce the possibility of errors. And they assure consistently high quality radiographs.

At left: A Tridoros Optimatic setup consisting of three examination units with their individual consoles. Any unit can also be operated from the master console at lower right.

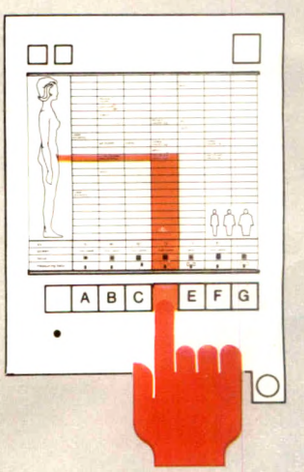
Below: Technician prepares for exposure by pushing desired organ-related button.



Pushbutton "B" sets typical Bucky table program for gall bladder, thin patient: 60kV, high-speed screen, small focal spot, Iontomat* center chamber.

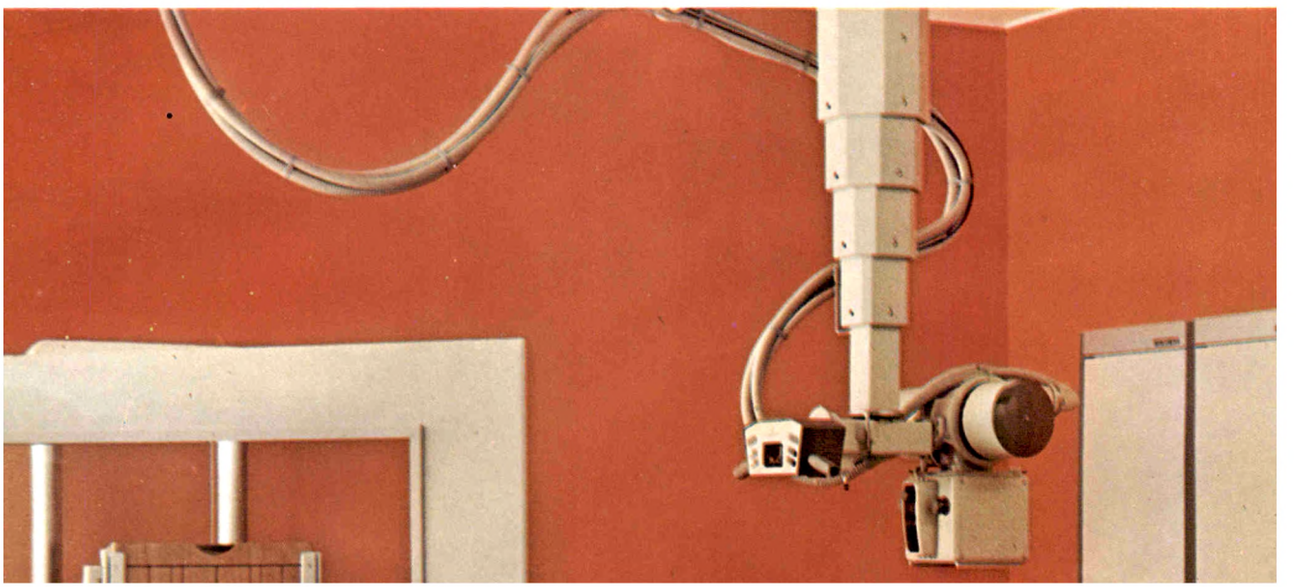


Pushbutton "E" sets typical Bucky table program for ribs 1-7, medium patient: 73kV, detail screen, small focal spot, Iontomat* center chamber.



Pushbutton "D" sets typical Bucky table program for sacrum and coccyx a.p., heavy patient: 73kV, high-speed screen, large focal spot, Iontomat* center chamber.

Now x-ray department layouts can be planned for optimum use of available space.



In many cases, where x-ray units are operated centrally from a console, compromises in the positioning of both the console and the examination units is necessary.

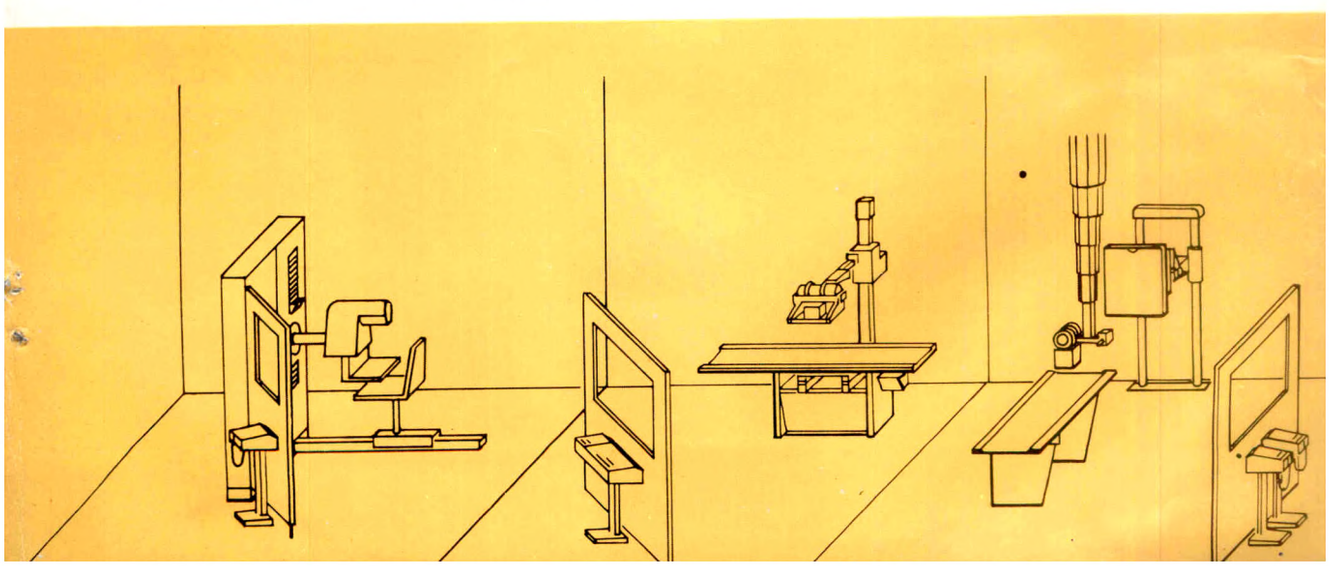
With the unit consoles of the Tridoros Optimatic system, the lay-out can be arranged in a more flexible manner.

In the setups shown below, technicians can preset pushbuttons either before or after positioning the patients. The actuated pushbuttons do not interfere with operation of other units. Only during the brief interval when an actual exposure is being made at one console is the use of the generator blocked for the other consoles. These exposure intervals are visually displayed by means of indicator lights on each console.

The new Siemens system permits the complete decentralization of any or all x-ray equipment. This is a significant advantage when an old installation is being modernized.

At left: Bucky wall stand and Bucky table with paired unit consoles.

Below: Four consoles are set up near the units they control. With this kind of arrangement and the automated exposure of the Siemens system, technicians can concentrate on patient positioning.

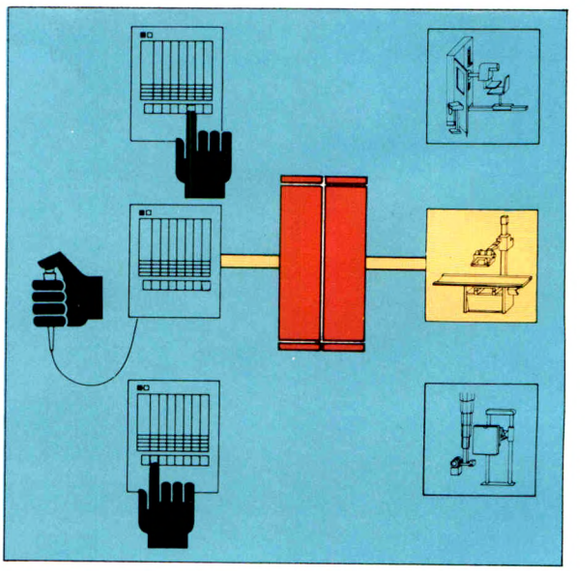


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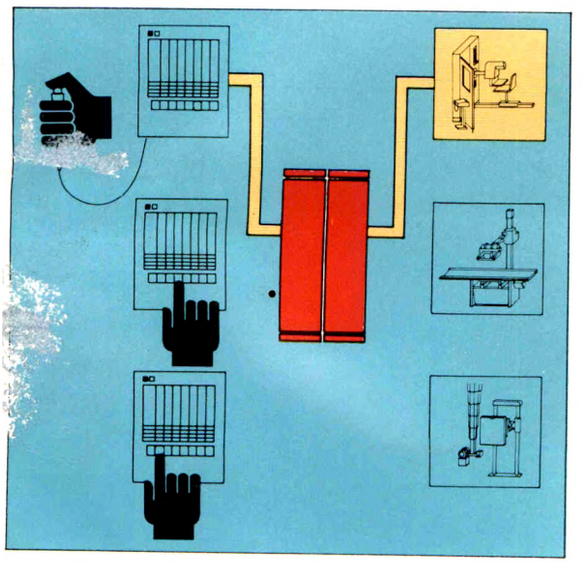
A new, practical way to improve the capability of your x-ray installation.

The Siemens Tridoros Optimatic system cuts to a minimum the number of decisions and adjustments technicians must make to get optimum results. Data selection and timing of all radiographic exposures are completely automated. And organ-related programs can be set simultaneously on several units.

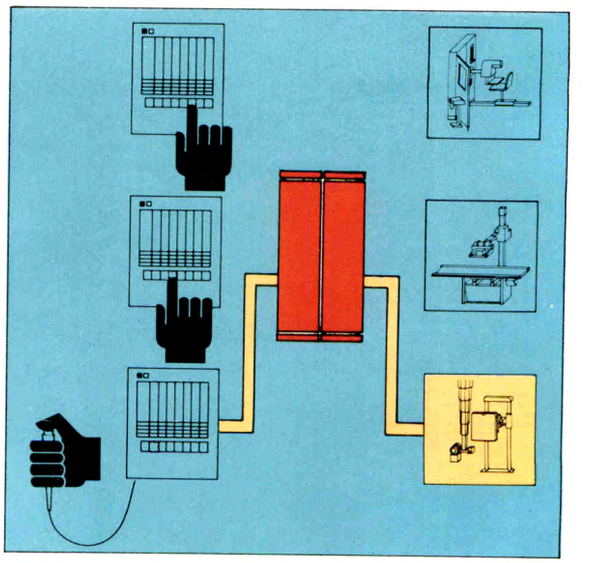
The preceding pages will give you an idea of how this new Siemens system can help you make the most efficient use of your radiological equipment and personnel. If you'd like to know more, please write Siemens Corporation, Medical Systems Division, 186 Wood Avenue South, Iselin, N.J. 08830.



(2) Programs for mammography and Bucky wall unit are selected while planigraphic exposure is made at unit console.



(1) Exposure is triggered for mammography while programs are selected at planigraphic table and Bucky wall stand.



(3) Third exposure is made at unit console controlling Bucky wall stand as programs are selected for the other two radiographic units.

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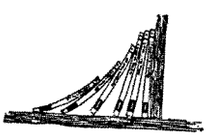
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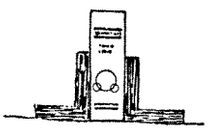
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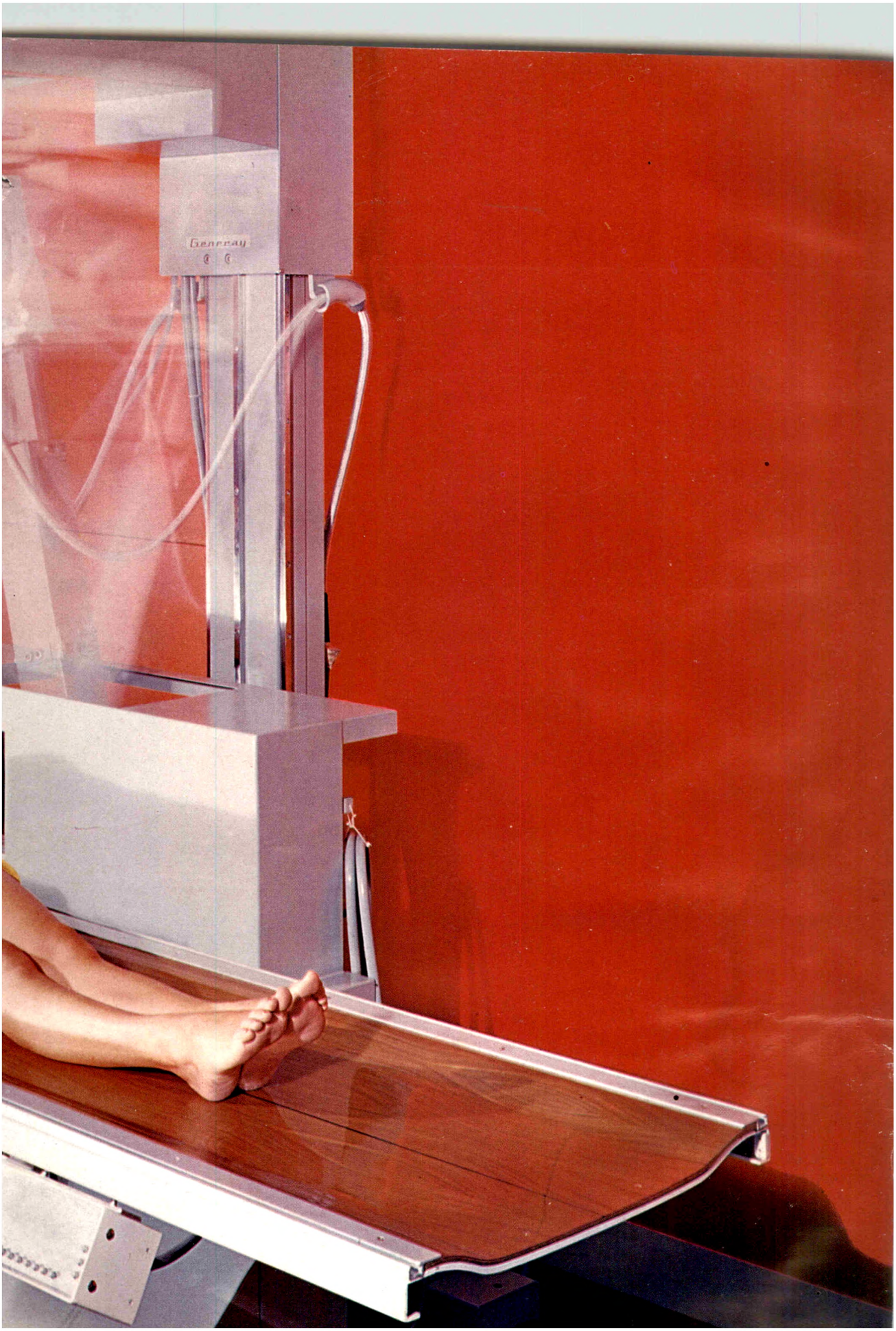
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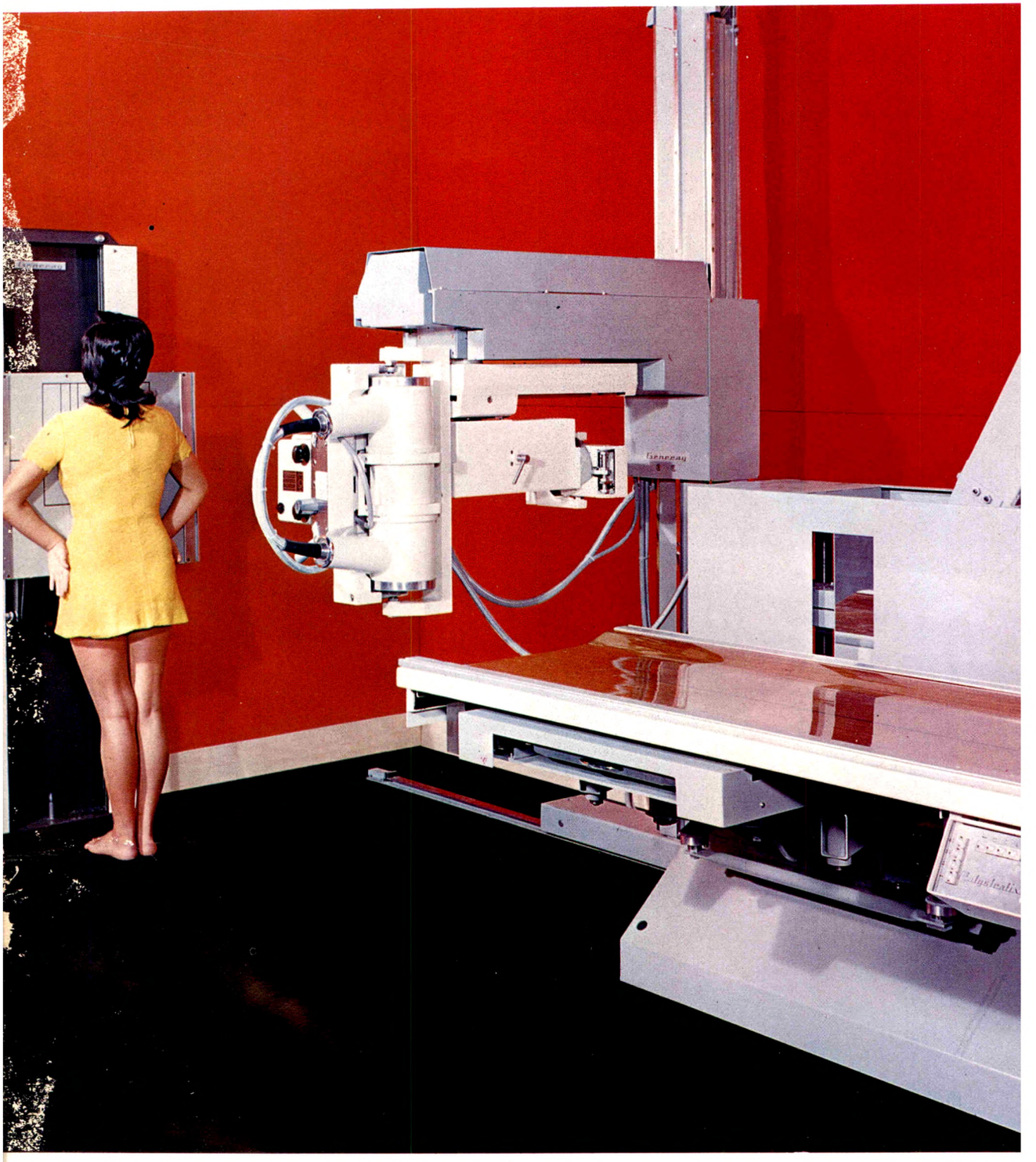




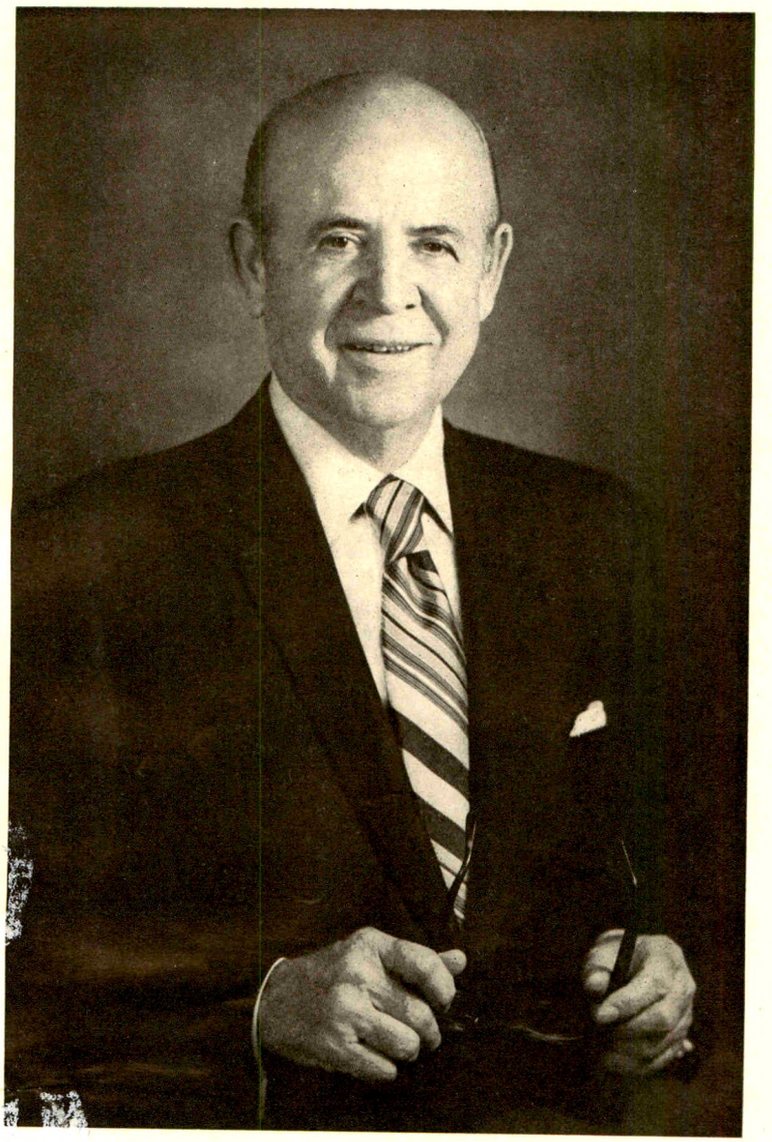

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JOHN V. BLADY, M.D.

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1972 PRESIDENTIAL REPORT TO THE MEMBERSHIP OF THE AMERICAN RADIUM SOCIETY*

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THE American Radium Society is an outstanding, time honored, 66 years young organization with an illustrious past. It hasn't changed much over the years even though progress in scientific medicine has made tremendous strides and marked changes have taken place in the socio-economic sphere.

With the advancement of scientific medicine, subspecialties within subspecialties are being achieved. As each subspecialty is established, a new Society is born. The field of organizations thus becomes highly competitive. Even though each has its specific purpose and value, it does engender fragmentation. Unfortunately the encroachment on the individual's time capacity and imposition of additional dues are deterrents to membership. Recognizing the changing scientific and economic atmosphere, it behooves us, therefore, to evaluate our organization.

In 1970 a mail questionnaire survey of the membership was conducted consisting of four items: 1. Type of Practice (Specialty or Subspecialty listing 13 categories); 2. Age; 3. Number of Years in Your Specialty; and 4. Meetings Attended During the Past Five Years (1966–1970). Three hundred and seventy (71%) replied out of a membership of 520 (451 Active, 15 Inactive and 54 Seniors).

The age spread was from 30 to 80 plus years. Seven members were in the 30–35 year group; 33 in the 36–40 year group; 43 in the 41–45 year group; and 53 in the 46–50 year group. The majority, 234 (64%), were in the 50 and over group.

Analyzing the years of experience with the age distribution gives us the following: In the 1 to 5 years practice group—9 members; 6 to 10 years—36; 11 to 15 years—5[illegible] 16 to 20 years—81; and 25 years and over—172.

Active membership in 1969–70 was 45[illegible] The attendance at Annual Meetings during the past five years on the basis of 370 returns (81%) was as follows: Attended all five meetings (1966–197[illegible] 5%; four meetings 13%; three meetings 25%; two meetings 41%; and one meeting 11%. T[illegible] eight per cent had not attended a [illegible] during the 1966–1970 period.

To summarize we may make the f[illegible] ing assumptions:

1. The Active Membership of the

* Presented at the Fifty-fourth Annual Meeting of the American Radium Society, in Joint Session with the James [illegible] and the Society of Head and Neck Surgeons, Boca Raton, Florida, May 14–19, 1972.

can Radium Society is 71% radiation oriented with only 21% surgeons and 3% internists.

2. Only 33% of the American Radium Society membership is under 50 years and only 7 members are in the 30–35 year group—1.5%.
3. The attendance at meetings is not consistent—only 5% attended all five meetings from 1966–1970. Forty-one per cent attended two meetings.

The tabulation of Type of Practice was the following:

1. Radiation Therapists	186
2. Radiation Therapy and Diagnosis	52
3. Diagnostic Radiology	11
4. Radiobiologists	3
5. Physicists	16
6. General Surgeons with Special Interest in Cancer	34
7. Gynecologists	26
8. Head and Neck Surgeons	15
9. Thoracic Surgeons	2
10. Urologists	2
11. Oto-Laryngologists	0
12. Medical Oncologists	6
13. Medical Education	2
14. Nuclear Medicine	3
15. Immunologists	1
16. Chemotherapists	2
17. Retirees and Unlisted	9

Our first concern must relate to the make-up of the American Radium Society. Are we satisfied with the type of practice distribution which we now have and have had for many years? Are we to duplicate or compete with the American Society of Therapeutic Radiologists and other related specialty Societies? Or are we to grow as an organization with primary interest in cancer in which all disciplines are adequately represented to make membership in the American Radium Society a desirable goal for all interested in cancer as it applies to all specialties?

In previous years attempts were made to interest our surgical confreres in our membership. This, however, has met with very slight success. Other means must be pursued in our approach to the surgeon. We also need to interest more internists and pathologists.

We should be exploring methods of encouraging younger membership, possibly by a junior type of membership which would confer limited privileges until full membership is attained.

Other facets to be explored include change in the name (not forgetting the purpose of its origin in 1916) and requirements for admission.

The objectives of the Society need to be brought into sharper focus of today's needs.

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TUMOR-FETAL ANTIGENS IN HODGKIN'S DISEASE: AN IMMUNOELECTROPHORETIC ANALYSIS*

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THE similarity of embryonic development and neoplasia has long been recognized,[3] but the relationship has received added attention only in recent years, following the discovery of the fetal antigens: alpha fetoprotein (AFP),[1,23] and carcinoembryonic antigen (CEA).[9,10] Alpha fetoprotein was isolated from normal fetal serum and from patients with primary hepatocellular carcinoma. The carcinoembryonic antigen was found in patients with digestive tract cancers and fetal digestive tract organs between 2 and 6 months gestation. Fetal antigens have also been associated with other human neoplasms arising in the breast,[7] stomach,[11] and brain.[24]

Hodgkin's disease is classified with the lymphomas,[15] but has several unique features. The disease often manifests a depressed cell-mediated immunity even when localized.[2,6] The histologic appearance is varied with a complex mixture of collagen, plasma cells, lymphocytes, granulocytes, eosinophils, recticulum cells, and Reed-Sternberg cells.[15] The malignant cells have been presumed by some to be Reed-Sternberg and reticulum cells,[20,22] although direct evidence of this is lacking. Often the majority of cells in a Hodgkin's disease "tumor" are lymphocytes, but it is not clear whether they are malignant, part of a host immune process, or both.

Recently, a tumor associated antigen in Hodgkin's disease was reported from this laboratory,[17] using a Hodgkin's disease heterologous antiserum and indirect immunofluorescence. Histocompatibility and species antibodies were removed by absorption with the normal region of the same patient's spleen. This technique demonstrated preferential antibody binding in Hodgkin's disease foci compared to the adjacent uninvolved spleen. Furthermore, the antigen was common to all of the patients studied. Further studies extended the immunofluorescence findings and identified a single precipitin band using a gel diffusion technique.[18] This precipitin band was not present in equal concentration in normal spleens.

The present study was designed to: (1) further define the antigens in Hodgkin's disease; (2) systematically survey a wide variety of other clinical diseases for the presence of such antigens; and (3) search for similar substances in fetal tissues. Tissue extracts were analyzed by immunoelectrophoresis, using a heterologous tumor antiserum absorbed with normal human spleen cells. Thus far 2 antigens have been identified in Hodgkin's disease tumors. These antigens were present in Hodgkin's disease tumors from a number of anatomic sites. They were also identified in embryonic liver, and spleens. When other pathologic processes involved the spleen, one antigen was found in 8 of 27 extracts analyzed, while the other was found in only 2. The data are analyzed and the relationship of fetal antigen and tumor associated antigens discussed.

MATERIAL AND METHOD

The Hodgkin's disease specimens used in this study were obtained during staging laparotomy, and splenectomy.[21] All tissue

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diagnoses were confirmed by microscopic examination. Fetal tissues were obtained from hysterotomy specimens or stillbirths, and specimens were assigned a number as received. Normal spleens were obtained at the time of surgery for other clinical indications.

ANTIGEN PREPARATION

Hodgkin's disease nodules in the spleen or lymph nodes were excised, weighed, and homogenized with a concentration of 1 gram of tissue per 5 ml. of normal saline which contained 0.035% disodium ethylene diaminetetraacetate (EDTA). Other surgical specimens and embryonic tissues were prepared in the same manner.

The crystalline samples of human serum proteins used in this study were obtained from the Miles Laboratories, Inc., and reconstituted with normal saline (with 0.035% EDTA) in the following concentrations: albumin 5 mg./ml.; alpha globulin (Fraction IV), 5 mg./ml.; beta globulin (Fraction III), 5 mg./ml.; and gamma globulin (Fraction II), 25 mg./ml.

ANTISERUM PRODUCTION

White New Zealand rabbits were immunized with splenic tumor extracts from individual patients. The antigen preparation contained from $2–4\times10^8$ nucleated cells and was mixed with an equal volume of complete Freund's adjuvant (Difco) and injected intradermally. Aliquots of the same extract were given as booster doses 14, 21 and 28 days after primary immunization. One week following the last injection, blood was obtained by cardiac puncture. The blood was kept sterile at room temperature for 1 hour, stored at 4° overnight to allow clot retraction, and the serum was separated and centrifuged at 900 revolutions per minute (RPM) for 10 minutes to remove the remaining red blood cells. The antiserum was heat inactivated at 56° for 30 minutes and stored at −20° C.

ABSORPTION OF ANTISERUM

Absorption of antiserum was carried out with 1×10^8 normal human nucleated spleen cells. One ml. aliquots of antiserum were incubated with the absorbing cells for 15 minutes, centrifuged at 900 RPM at 4° C. for 10 minutes, and the supernatant collected and tested for reactivity with the standard control antigens. Further absorptions were done when negative controls registered precipitin bands on immunoelectrophoresis. Absorption was considered complete when negative controls did not yield precipitin bands.

IMMUNOELECTROPHORESIS

Immunoelectrophoretic analysis was accomplished using agarose plates equilibrated with 0.05 M sodium barbital buffer, pH 8.6 with 0.035% EDTA and the same buffer was used in the electrophoresis chamber. The electrophoresis chamber, agarose plates, stains, and buffer were all obtained from Analytic Chemists, Inc. The 8 antigen sample wells were loaded twice with a microliter dispenser which delivered 1 lambda. The antigen wells were located at the cathode and 100 ml. of 0.05 M barbital buffer pH 8.6 with 0.035% EDTA were placed in the chamber surrounding each electrode. The plates were subjected to a potential difference of 15 volts/cm. for 35 minutes and removed. Antibody troughs were filled twice with a total of 40 lambda of absorbed antiserum. Immunodiffusion occurred over 48 hours and the plates were then equilibrated with saline for 90 minutes, fixed with 0.1% tannic acid for 10 minutes, stained in 0.2% 8-anilino-1-naphthalenesulfonic acid (ANSA) for 10 minutes, rinsed in 5% acetic acid for 1 minute, and dried at 90° C. for 25 minutes. The dry plates were photographed with Polaroid type 42 film, using indirect lighting, and the photographs scored for the presence or absence of precipitin bands and their position relative to the antigen well.

CONTROLS

Each plate contained 8 antigen wells. Two wells contained nonreacting normal controls, 2 wells contained positive reacting

Hodgkin's disease tumor extracts and the remaining 4 were loaded with the test antigens (Fig. 1). These controls were adopted to guide the level of absorption required to remove antibodies to normal human antigens, but retain antibodies to antigens associated with the tumors.

RESULTS

Immunoelectrophoresis has resolved 2 antigens as shown in Figure 1. We have labeled these fast (F) or slow (S) according to their electrophoretic mobility. The fast antigen was located 16 mm. and the slow antigen 12 mm. from the antigen well. All plates had 2 negative controls, 2 positive controls, and 4 test antigens. The controls were necessary to assure appropriate sensitivity. The presence of either precipitin line was recorded as a positive result (Fig. 1).

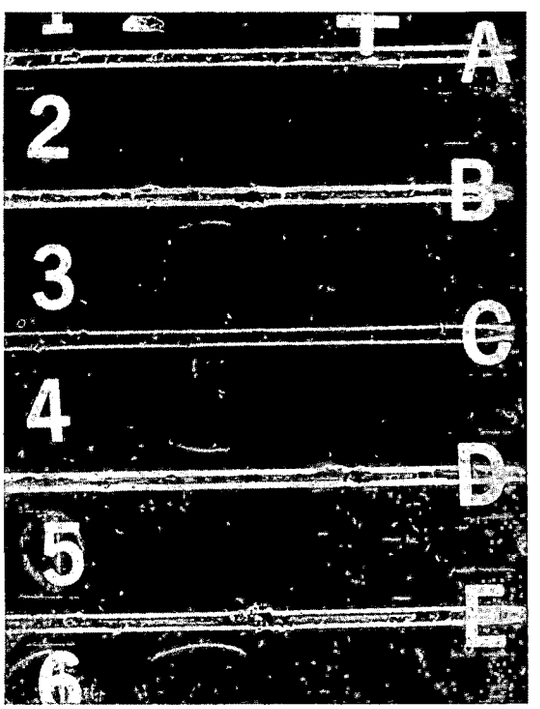


Fig. 1. Section of immunoelectrophoresis plate to demonstrate use of controls and S and F antigens. The cathode is on the left and the anode on the right. Wells 1 and 2 contained extracts of normal spleen antigen and show no reaction. Wells 3 and 4 contained the positive tumor controls. The extract placed in well 5 contained only the S antigen, while well 6 contained only the F antigen.

Table I

Immunoelectrophoresis of Hodgkin's Disease Splenic Tumors

Antigens	No. of Patients	Histology
F	13	3 LD 5 MC 5 NS
SF	9	3 LD 3 MC 3 NS
O*	1	1 MC
Total positive reactions	22/23	

Controls consisted of 2 negative normal splenic extracts and 2 positive Hodgkin's disease splenic extracts. The tumor antiserum was absorbed with normal spleen cells.

Abbreviations used: MC, mixed cellularity; NS, nodular sclerosis; LD, lymphocyte depleted; U, unclassified; S, slowly migrating antigen; F, fast migrating antigen; O, no reaction.

* The slides were reviewed by another pathologist. His diagnosis was nodular lymphoma rather than Hodgkin's disease.

Extracts of Hodgkin's disease nodules excised from the spleen gave a positive reaction in 22 of 23 patients (Table 1).* There was no apparent correlation of precipitin band type with histologic type or clinical stage. When the Hodgkin's disease involved lymph nodes, 5 of 6 extracts contained the antigens (Table II). The normal regions of 4 Hodgkin's disease containing spleens were analyzed and a positive reaction was seen in 1 (Table III). Occasionally spleens from patients with Hodgkin's disease revealed changes suggesting Hodgkin's disease, but Reed-Sternberg cells could not be identified; of 4 such histologically suspicious spleens analyzed 3 gave a positive reaction (Table III). Histologically normal spleens from patients with Hodgkin's disease contained the antigens in 7 out of 14 instances (Table III). The F antigen was also found in a mass of Hodgkin's disease resected from the lung.

* The slides of the 1 specimen that did not react were reviewed by another pathologist. His diagnosis was nodular lymphoma rather than Hodgkin's disease.

TABLE II

IMMUNOELECTROPHORESIS OF HODGKIN'S DISEASE LYMPH NODE TUMORS

Antigens	No. of Patients	Histology
S	4	2 LD 1 NS 1 U
SF	1	1 MC
O	1	1 NS
Total positive reactions	5/6	

Abbreviations same as in Table 1.

There were no detectable antigens in Hodgkin's disease tissue resected from the spinal canal of a patient treated with chemotherapy.

Spleens and lymph nodes were analyzed from patients with a variety of other clinical illnesses. Six of 27 spleens showed only the F antigen, while 2 contained both antigens (Table IV). A positive reaction was not seen among the lymph nodes from 5 patients (Table V). Only 1 adult liver specimen has been available for analysis and neither the S nor F antigen could be found.

Fetal and newborn tissues were also analyzed and the antigens were detected in 8 of 8 livers, 3 of 4 spleens, and 1 of 7 thymus glands tested (Table VI). No reaction was seen for the following: fetal gut 0/2; fetal lung 0/3; fetal muscle 0/1; amniotic fluid 0/1; or placenta 0/1.

The results of electrophoretic mobility studies which compared normal serum proteins to tumor associated antigens are charted in Table VII. The center of the migrating ellipse of the F antigen moved 16 mm., S antigen 12 mm., alpha globulins 18 mm., beta globulins 6 mm., and gamma globulin 0 mm. This indicates that these tumor associated antigens are different than the major serum proteins.

DISCUSSION

The tumor-fetal F antigen was most prominent in splenic Hodgkin's disease, fetal hematopoietic tissue, and disease processes suggesting abnormal immunity. The presence of an antigen not normally found in significant concentration in adult tissues was not only associated with active malignancy, but was found in 7 out of 14 histologically negative spleens removed from Hodgkin's disease patients. This latter finding must be interpreted with caution, but may suggest that antigenic alteration precedes histologic recognition of involvement by Hodgkin's disease. Alternatively, the response may be 'reactive,' similar to that seen in the spleens removed from the patients with lymphoid hyperplasia.

The S antigen was found in the most immature fetal liver and in the only neonatal thymus analyzed. It was also present in all Hodgkin's disease lymph node extracts. Thus the S antigen was more restricted in distribution and appears to be related to Hodgkin's disease rather than to other illnesses.

TABLE III

IMMUNOELECTROPHORESIS OF OTHER SPLEENS FROM HODGKIN'S DISEASE PATIENTS

Histology	No. of Patients	Antigens
Normal region	1/4	1 F 3 O
Suspicious	3/4	2 F 1 SF 1 O
Negative	7/14	4 F 1 S 2 SF 7 O

Controls and abbreviations same as in Table 1.

Normal region refers to an uninvolved area of a spleen that contained Hodgkin's disease. Suspicious refers to spleens that had changes suggesting Hodgkin's disease, but Reed-Sternberg cells could not be identified. Negative spleens were thin sliced and multiple sections analyzed without finding evidence of Hodgkin's disease.

TABLE IV

IMMUNOELECTROPHORESIS OF SPLEENS FROM OTHER CLINICAL STATES

Clinical Indication	Histology	Antigens
Peptic ulcer	Normal	o
Pancreatitis	Normal	o
Dx. lap.	Lymphosarcoma	o
Myelofibrosis	Myeloid metaplasia	o
Portal hypertension	Chronic congestion	o
H.d. and Infect. mono.	Lymphoid hyperplasia	o
Carcinoma of esophagus	Normal	o
Teratocarcinoma of testis	Normal	o
ITP	Follicular hyperplasia	o
Portal hypertension	Fibro congestion	o
ITP	Normal	o
Diverticulitis of colon	Normal	o
Hiatal hernia	Normal	o
ITP	Normal	o
ITP	Lymphoid hyperplasia	o
Renal cell carcinoma	Normal	o
Carcinoma of esophagus	Normal	o
Hiatal hernia	Normal	o
CGN	Normal	o
Splenic rupture	Normal	SF
Peptic ulcer	Heterotopic bone formation	F
Aplastic anemia	Plasma cells, histiocytes	F
ITP	Hyperplastic follicles	F
Hiatal hernia	Normal	F
CGN	Lymphoid hyperplasia	F
Anemia, leukemia	Lipid granuloma	F
Splenomegaly	Sarcoid	SF
		8/27

Abbreviations used: o, no reaction; Dx. lap., diagnostic laparotomy; H.d.-Infect. mono., patient eventually determined to have both infectious mononucleosis and Hodgkin's disease; ITP, idiopathic thrombocytopenic purpura; CGN, chronic glomerulonephritis.

The possible inciting agent for the expression of the tumor-fetal antigens remains unknown. The possibilities of viral

TABLE V

IMMUNOELECTROPHORESIS OF LYMPH NODES FROM OTHER CLINICAL STATES

Clinical Indication	Lymph Node Histology	Antigens
Uterine fibroids	Normal	o
Lung carcinoma	Squamous cell carcinoma	o
Carcinoma of esophagus	Adenocarcinoma	o
Lung lesion	Sarcoid	o
Lung lesion	Sarcoid	o
		o/5

Controls and abbreviations same as in previous Tables.

TABLE VI

IMMUNOELECTROPHORESIS OF FETAL ANTIGENS

Gestation Age (Weeks)	Liver	Spleen	Thymus
8	S	—	—
10	F	F	o
10	F	o	o
12	F	—	—
15	F	—	o
19	F	—	o
32	F	F	o
40	F	F	o
40*	—	—	FS
	8/8	3/4	1/7

(—) Tissue was not available. Other abbreviations same as in previous Tables.

* Term infant who died 2 weeks after birth.

TABLE VII

ELECTROPHORETIC MOBILITY

Precipitin Arc	Migration Distance (mm.)*
Gamma globulins	0†, 7
Beta globulins	6†, 10, 11
Slow antigen	12
Fast antigen	16
Alpha globulins	10, 18 , 20, 25
Albumin	25

* The migration distance is recorded as the center of the precipitin arc.

† The predominant band if others were present.

agents, immune reactions, or both, remain to be studied. Recent preliminary studies using immunofluorescence of live cell suspensions suggested that F antigen was associated with a subpopulation of lymphocytes. This finding in conjunction with cryostat sections previously reported[17,18] suggests that F antigen may be a cell surface antigen.

Thus S and F antigens may be related to specific classes of cells present in excess in Hodgkin's disease. For example, F antigen may be related to reactive lymphocytes and be exposed when such cells are actively proliferating. This would explain its appearance in other diseases with immunologic abnormality. Studies with tritiated thymidine suggest that large lymphocytes or "lymphoblasts" as well as early reticulum cells were actively synthesizing DNA and therefore were the proliferating cells.[20] A pathogenesis of Hodgkin's disease was hypothesized which accounts for the presence of chronically active proliferating thymus derived lymphocytes (T cells) and malignant reticulum cells consistent with these findings and is reported elsewhere.[19]

The majority of cells in a focus of Hodgkin's disease are probably reactive cells and the same type of cells could respond to other disease processes, thus giving an occasional positive reaction. Similarly, fetal liver and fetal spleen are hematopoietic organs[25] and could produce the same cells or possibly expose the same proliferation antigens.

Detection of these antigens in other clinical states indicates that the precipitin bands observed by this technique were not tumor specific, but were tumor associated. Tumor associated antigens are normal tissue antigens increased in concentration or appearing in a new location due to the disease process. Such antigens have been identified in fetal tissues as in alpha fetoprotein, carcinoembryonic antigen, and now Hodgkin's disease. Alpha fetoprotein and carcinoembryonic antigen have also been noted in significant concentrations in other diseases and therefore are tumor associated antigens as well.

CONCLUSION

The study of such antigens in Hodgkin's disease may help in elucidating some of the features of the malignant process and the host's response to it.

For the practicing oncologist, however, the presence of potentially measurable serologic levels of tumor associated antigens would yield valuable information as to recurrence or reactivation of disease.

This would be particularly helpful in patients with Hodgkin's disease treated with chemotherapy or irradiation.

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SURGICAL ASPECTS AND RESULTS OF LAPAROTOMY AND SPLENECTOMY IN HODGKIN'S DISEASE*

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SINCE laparotomy and splenectomy have come to be heavily relied upon for accurate staging of patients with Hodgkin's disease, it is particularly important to review the surgical experience with reference to technique, limitations, morbidity and complications of the surgical procedure. Fifty-one patients with Hodgkin's disease who underwent laparotomy and splenectomy at Memorial Hospital for Cancer and Allied Diseases during the 2 year period September 1969 through August 1971 are the basis for this review.

Hodgkin's disease which can involve the lymphatic tissues anywhere in the body has been a source of frustration for clinicians in their attempt to determine the extent of the disease and thereby plan appropriate therapy. Initially, therapy was directed only to those areas where disease could be palpated or seen by standard roentgenologic techniques.

Lymphangiographic studies to visualize retroperitoneal lymph nodes improved the accuracy of diagnosis, but the upper abdominal lymph nodes between the second lumbar vertebra and the diaphragm could not be visualized, and accurate preoperative evaluation of the spleen and liver continued to elude us. In addition, it became apparent that lymphangiographic interpretation could not always be relied upon.

Because of the need for more accurate diagnosis with regard to the presence or absence of Hodgkin's disease below the diaphragm, a prospective study was started at Memorial Center in September 1969. Although at that time no published data existed regarding the findings of the Hodgkin's Disease Study Group of the Stanford University School of Medicine, direct communication with them indicated that at least 65 patients had already been operated on for splenectomy, liver biopsy and selected lymph node biopsies. In October 1969, a report was given by Glatstein *et al.*[3]

Since Glatstein's publication, further studies from the Stanford Group,[3,7,8] Jelliffe *et al.*,[6] Aisenberg *et al.*,[1] Lowenbraun *et al.*,[9] Allen and Ultman,[2] Prosnitz *et al.*,[11] and Goldman[5] have confirmed the value of the staging laparotomy and splenectomy in Hodgkin's disease.

METHOD (TABLE I)

Patients with Hodgkin's disease were admitted to the study by physicians on the Medical Oncology Service. During the 2 year period, September 1, 1969 through August 31, 1971, 2 groups of patients underwent surgery. Group I consisted of 40 patients submitted for surgery as part of their initial staging. Group II, comprised of 11 patients, underwent surgical staging after tumor free intervals of 1 to 8 years following initial therapy. Each of the patients in

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TABLE I

STAGING LAPAROTOMY

(1969–1971)

	No.
Group I	
No previous treatment	40
Group II	
Previous diagnosis of Hodgkin's disease 1–8 years ago	
Previous treatment	11
Total	51

Group II was being restaged because of tumor recurrence. The age group ranged from 15 to 62 years; the majority of the patients were in the 20 to 40 year age range. The pediatric age group will be reported elsewhere.

Preoperative work-up included complete history and physical examination with special attention to systemic symptoms (fever, pruritus) and signs of lymph node enlargement or hepatosplenomegaly. Laboratory studies done included screening chemistries, liver chemistries, complete blood cell count, platelet count, chest roentgenography, electrocardiography, intravenous pyelography, and lymphangiography (unless contraindicated by sensitivity to iodine). After initial examinations, patients were evaluated and staged clinically according to the classification proposed by the conference on Hodgkin's disease at Rye, New York, 1965.

Prior to surgery, a review of the lymphangiogram by the radiologist, medical oncologist, and surgeon was undertaken in an effort to agree on the periaortic lymph nodes for biopsy at the time of surgery.

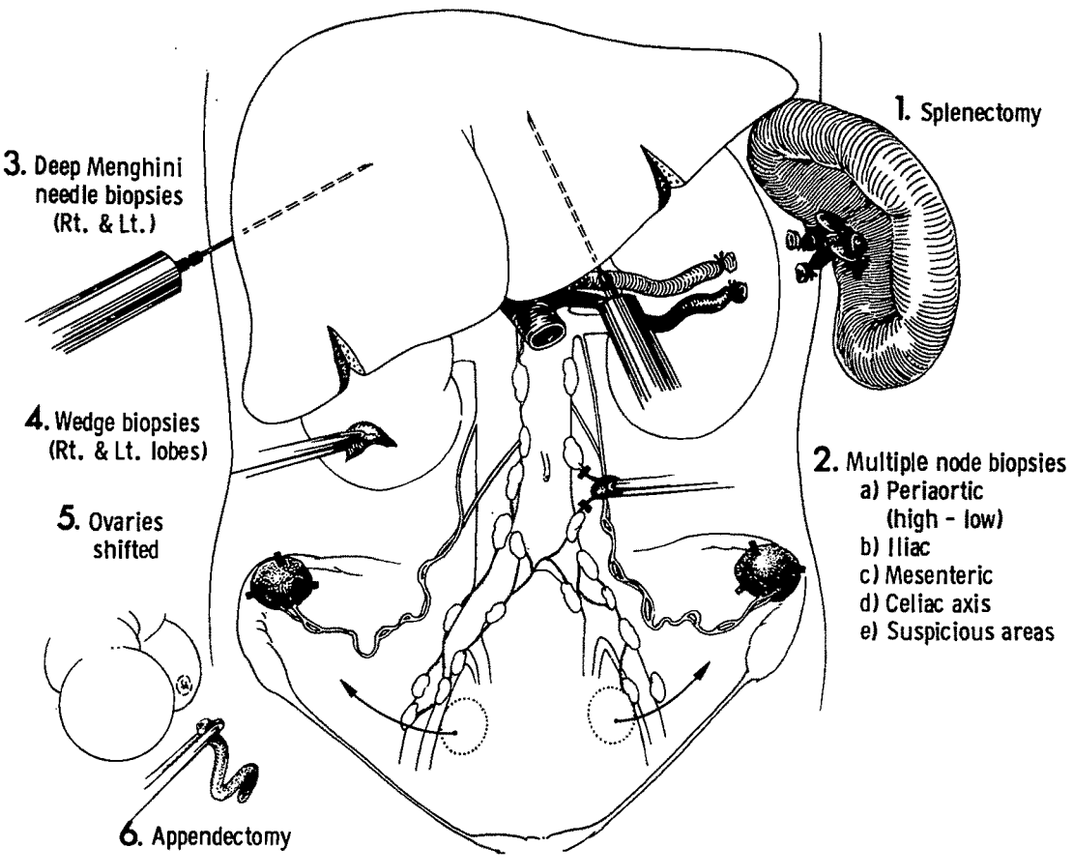


FIG. 1.

This was in addition to the routine selected lymph node biopsy sampling of all areas from the celiac axis down to the lymph nodes at the level of the iliac arteries.

TECHNIQUE

The operative approach has been through a left paramedian incision, and the following steps were carried out (Fig. 1).

1. Careful abdominal exploration to evaluate not only the lymph nodes, spleen, liver and ovaries, but also to inspect for the presence of Hodgkin's involvement of any other organ. If found, appropriate biopsies were taken.
2. Splenectomy was then performed and included the removal of the splenic hilar lymph nodes. The usual surgical approach was first the division and ligation of the short gastric vessels. Next, division of the splenocolic and splenorenal ligaments. This was followed by incision of the posterior peritoneum over the kidney and elevation of the tail of the pancreas and spleen into the operative field, so that the splenic artery and vein could be individually isolated and ligated. This allows for dissection and removal of the splenic hilar lymph nodes and removal of the spleen with a long splenic pedicle. It further allows excellent visualization of the tail of the pancreas to avoid unnecessary injury to this organ. A large single metallic clip should be placed on the splenic artery stump for identification purposes. Placement of small metallic clips in the left upper quadrant for hemostasis will often lead to confusion in placement of radiation portals over the splenic artery. Experience has shown that the use of a single large clip on the splenic artery will clarify the situation.
3. Wedge biopsies of the right and left lobes of the liver are taken from the leading liver edges. If any suspicious areas are noted, then biopsies of these are also taken. In addition, deep Menghini needle biopsies are taken from the central deep areas of the right and left liver lobes.
4. Periaortic lymph node biopsies are then taken of any suspicious lymph nodes seen on the lymphangiogram or by direct clinical inspection. This is in addition to the extensive lymph node sampling according to the check-off list. Exposure of the periaortic region is obtained by displacing the transverse colon and small bowel outside the abdominal cavity and then incising the mesentery of the colon below the duodenum and medial to the inferior mesenteric vein. By elevation of the fourth portion of the duodenum, the periaortic lymph nodes to the level of the renal vein are exposed. All sites of the periaortic lymph node biopsies are marked with hemostatic silver clips which assist in both lymph- and hemostasis and serve to identify the areas where lymph nodes were removed on follow-up roentgenograms of the abdomen. An attempt is also made to indicate the lateral extent of the lymph node masses in the periaortic areas to assist the radiation therapist with future treatment planning. Roentgenograms may be taken during the course of the procedure to help insure the removal of suspicious lymph nodes initially seen on the lymphangiogram. The lymph nodes removed at surgery are submitted for frozen section. Often Hodgkin's disease can be identified as well as the "lymphangiogram effect." The latter diagnosis is helpful in being certain that the lymph nodes removed are also the lymph nodes that were visualized on the preoperative roentgenograms.
5. Biopsies are done of any mesenteric, celiac or other suspicious lymph nodes noted at the time of surgery.
6. In young women in the child-bearing age, transfer of one or both ovaries

from the pelvis has been carried out. Should there be any future radiotherapy to the pelvis, this eliminates an artificial menopause. Lateral ovarian transposition from the true to the false pelvis according to the methods of J. L. Lewis, Jr.[10] has been the preferred method of transfer. This will best remove the ovary from any future radiation beam and help preserve ovarian function. Ovarian transfer can be done by carefully dividing the mesovarium, leaving the infundibulopelvic blood supply to the ovary intact, and then suturing the ovary to a region over the anterior iliac crest. The Fallopian tubes are left behind attached to the uterus in the true pelvis. Our policy is to mark the ovary with 3 silver clips for future identification. In this series of patients, 1 patient who has had both ovaries moved laterally to the iliac crest areas is now pregnant. A less desirable area to transfer the ovary to is behind the uterus. This offers less protection from radiation therapy and, on occasion, patients have complained of pelvic pain during sexual intercourse.

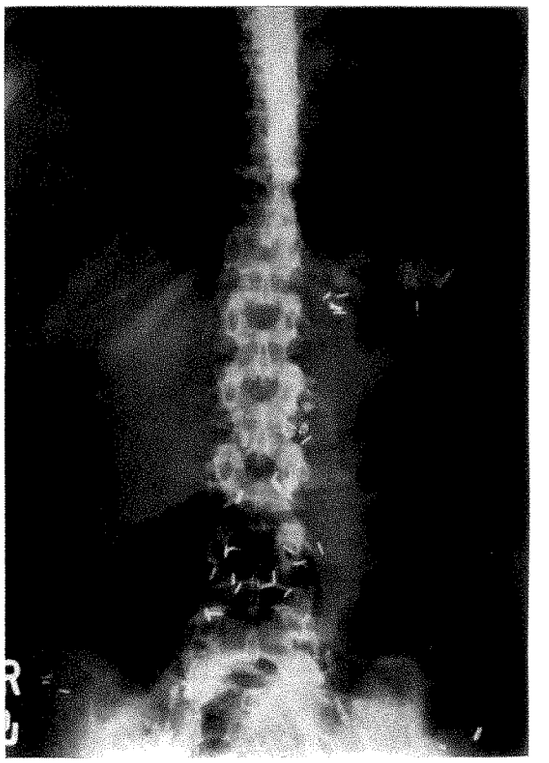


FIG. 3.

CHECK LIST

EXPLORATORY LAPAROTOMY FOR HODGKIN'S DISEASE

Patient's name _____ Date _____

Chart no. _____

Attending physicians _____

	Yes	No
Lymphangiogram reviewed for node sampling?	☐	☐
Laparotomy monitored with fluoroscopy or films?	☐	☐
Splenectomy?	☐	☐
Clips placed on pedicle?	☐	☐
Biopsies: Bone - iliac crest	☐	☐
Biopsies: Liver - right lobe - wedge	☐	☐
Biopsies: Liver - right lobe - needle	☐	☐
Biopsies: Liver - left lobe - wedge	☐	☐
Biopsies: Liver - left lobe - needle	☐	☐
Node sampling - indicated in diagram?	☐	☐
Clips placed?	☐	☐
Right external iliac	☐	☐
Left external iliac	☐	☐
Right common iliac	☐	☐
Left common iliac	☐	☐
Lower lumbar L2 - L4	☐	☐
Upper lumbar (renal pedicle)	☐	☐
High retroperitoneal (celiac axis)	☐	☐
Splenic hilus	☐	☐
Mesenteric	☐	☐
Oophoropexy?	☐	☐
Clips placed on either pole?	☐	☐
Repositioned: lateral and up?	☐	☐
Repositioned: midline?	☐	☐



FIG. 2.

7. Finally, appendectomy is carried out, since patients with Hodgkin's disease will on occasion develop gastrointestinal involvement and abdominal pain. It also seems desirable to remove the appendix at the time of laparotomy, so that confusion between Mittelschmerz pain (from a transposed ovary) and appendicitis is avoided.
8. At completion of surgery, a check list is gone over prior to closure (Fig. 2). Postoperative plain roentgenograms of the abdomen are taken to: (1) determine whether the suspicious areas have been biopsied; (2) identify the placement of the ovaries; and (3) identify the distal end of the splenic artery by the operatively placed metallic clip (Fig. 3).

TABLE II

CHANGE IN STAGING AFTER LAPAROTOMY
(1969–1971)

Clinical	Post Surgery		
	No Change	Stage Up	Stage Down
Stage I (11)	10	1 (III)	—
Stage II (9)	4	5 (III)	—
Stage III (12)	5	1 (IV)	6 (II)
Stage IV* (8)	2	—	6 (II[2]) (III[4])
• 40	21	7	12

* 6 liver, 1 bone, and 1 lung involvement.

ADVANTAGES AND LIMITATIONS

The advantages and limitations of the operative procedure may be best appreciated by reviewing the results in the 40 patients of the primary staging group. In the primary group of explored patients, a summary of the changes in staging after laparotomy, splenectomy, lymph node and liver biopsy appears in Table II. The significant changes of either increasing or decreasing the stage occurred predominantly in Stages II through IV. In the Stage IV patients, 6 out of 8 patients were changed to a lesser stage because of the failure to confirm liver involvement. In 6 out of these 8 patients originally believed to have Hodgkin's disease in the liver (because of increased alkaline phosphatase, increased SGOT, increased 5' nucleotidase, or palpable liver, or a combination of these findings), biopsy confirmation did not occur. This again demonstrates the difficulty in making a preoperative assessment of liver involvement with Hodgkin's disease.

The 2 patients originally diagnosed as Stage IV, who remained so postoperatively, did so because the Stage IV diagnosis was related to lung disease in one case and bone disease in the other, and the operative abdominal findings did not influence the staging. One patient was advanced to Stage IV from Stage III because of the discovery of liver involvement at surgery.

The spleen remains a source of cryptic tumor, and in Table III the results of this series are compared with previously reported studies. In this series, 9 out of 37 patients with clinically anticipated normal spleens were found to have tumor (Table IV). The percentage changed from negative to positive because the results of surgery are slightly lower in this series than in the other studies reviewed. The implication remains clear, however: from 2 to 5 out of every 10 patients with Hodgkin's disease will have tumor in their spleen at the onset of their disease, although clinically it cannot be detected. This number will vary from series to series.

Lymphangiography has proven to be a very useful procedure in the preoperative assessment of the patient (Table IV). There may have been a certain degree of "over reading" in the 4 suspicious cases, as they all turned out to be negative. However, what is not stated in this type of analysis is the fact that the surgeon frequently cannot obtain the lymph nodes the clinician wants him to sample. More important, in terms

TABLE III

RESULTS OF STAGING LAPAROTOMY
UNSUSPECTED HODGKIN'S DISEASE IN THE SPLEEN

Study Group	Surgical Positive/ Clinical Negative	Per Cent Change Negative to Positive
Memorial Hospital NYC (1969–1971)	9/37	24.3
Stanford University	10/38	26.3
Yale University	15/38	39.4
University of Chicago	5/17	29.4
Massachusetts General Hospital	9/19	47.4

of the positive effect of the surgery, are the patients whose preoperative lymphangiograms were definitely "negative" or normal appearing, but whose lymph nodes turned out to be positive for Hodgkin's disease on surgical sampling. The postoperative usefulness of follow-up roentgenograms in this setting cannot be overemphasized. The lymphangiographic contrast material remains for about 1 year in most patients and serves to delineate what was done at surgery and what is occurring in the postoperative period.

The failure to obtain adequate lymph node samples must be anticipated, even in the adequately explored patient. In some patients the nodal tumor is diffuse and hard and only wedge resection from selected areas can be done. In one instance, the extent of pancreatic involvement was so extreme that the removal of the spleen (that subsequently was declared free of tumor by the pathologist) was almost abandoned because of technical problems of mobilization of the spleen under these adverse circumstances. This was a totally unsuspected and unanticipated problem preoperatively.

We are also certain that, although surgery implied that the lymph nodes were "negative" in patients in whom the lymphangiogram was clearly positive, some of these patients definitely have Hodgkin's disease below the diaphragm despite the "negative" exploration. This, of course, has been proven by follow-up of the patient who had obvious progressive disease subsequent to surgery. In other words, the surgeon can and does miss obviously positive lymph nodes that were seen initially on the initial lymphangiogram.

MORTALITY AND MORBIDITY

In the 51 patients operated there were no deaths. The anticipated morbidity included: (1) postoperative tachycardia 100 to 120 per minute, believed to be secondary to pooling of body fluids into retroperitoneal spaces and usually responding to adequate fluid and colloid replacement;

TABLE IV

STAGING LAPAROTOMY

(1969–1971)

Clinical Interpretation	Surgical Results		
Lymphangiogram	*Periaortic Lymph Node Sampling*		
Positive or Suspicious 12 (4)	Positive 10	Negative 2(4)	NB —
Negative 23	4	17	2
Not Done 1*	—	1	—

* Iodine sensitivity. NB = no biopsy.

(2) postoperative ileus lasting 4 to 7 days; (3) incisional pain of 4 to 7 days' duration; (4) postoperative lung atelectasis, especially at the bases, of minimal degree; (5) small left basilar pleural effusion may occur which is sterile and resolves without special therapy. Postoperative antibiotics were not used routinely. Most of the expected morbidity resolved with supportive routine postoperative care. The average hospital stay following laparotomy staging for Hodgkin's disease was 10 to 11 days to discharge.

Pre- and postoperative fever of Hodgkin's disease origin was controlled with indomethacin. Postoperatively indomethacin was administered rectally every 4 to 6 hours by placing 25 mg. to 50 mg. of indomethacin powder in rectal glycerine suppositories. This was continued until the indomethacin could be taken orally postoperatively.

COMPLICATIONS (TABLE V)

Serious complications immediately postoperatively included left subphrenic abscess and right lower lobe pneumonia in 1 patient. These were treated with antibiotics and surgical drainage.

Five patients developed 7 late complications. These included:

1. Incomplete small bowel obstruction and left thigh phlebitis in the same patient 4 months after laparotomy

TABLE V

COMPLICATIONS OF LAPAROTOMY—SPLENECTOMY (1969–1971; 51 patients)

Immediate postoperative	
1 patient	Left subphrenic abscess, pneumonia
Late postoperative	
5 patients	
1. Incomplete small bowel obstruction, phlebitis (4 mo.)	
2. Cystitis, suture granuloma (1 mo.)	
3. Cecal abscess, peritonitis (9 mo.)	
4. Wound abscess (1 mo.)	
5. Ventral hernia (6 mo.)	

and following a course of multiple drug therapy; both complications resolved without surgery employing conservative measures

2. One patient developed a suture granuloma and cystitis
3. One patient with Stage IV Hodgkin's disease developed a peritonitis secondary to a perforation of a cecal bowel abscess 9 months after laparotomy and 3 months after completion of a course of multiple drug chemotherapy
4. One patient developed a wound abscess 4 weeks postoperatively; this responded to drainage and antibiotics
5. One patient developed a ventral hernia 6 months after initial laparotomy.

SUMMARY

Surgical staging of Hodgkin's disease, *i.e.*, laparotomy and splenectomy is a complex procedure, requiring considerable preoperative preparation and anticipation by the surgeon in conjunction with his medical colleagues.

The surgeon is responsible for the systematic removal of the spleen, liver biopsy samples, lymph node samples, removal of the appendix and transposition of the ovaries in the female patient.

He must adequately and systematically mark these areas of dissection to assist later in the evaluation of the pathologic findings and to assist the radiation therapist in treatment planning when that is performed postoperatively.

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CLINICAL COURSES OF HODGKIN'S DISEASE AND OTHER MALIGNANT LYMPHOMAS*

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IN the past decade great progress has been made in the diagnosis and treatment of malignant lymphomas. Although many reports[4] have appeared correlating the natural history of Hodgkin's disease with the Luke's pathologic classification and the staging system proposed at the Rye Conference in 1965, very few similar detailed studies have been made with other malignant lymphomas.

It is believed that the similarities and differences of the clinical courses of Hodgkin's disease and other malignant lymphomas can be better demonstrated by studying them side by side. Therefore, we conducted a detailed and comprehensive review of all patients with the diagnosis of Hodgkin's disease, reticulum cell sarcoma, lymphosarcoma and unspecified lymphoma admitted to a single institution in the past 30 years.

This report summarizes the information from this analysis as it pertains to the age and sex distribution of the group, the clinical stages, the histologic classification, the results of therapy, and the prognosis and survival of various subgroups.

CLINICAL MATERIAL

This is a retrospective and all-inclusive study of 591 patients who were seen and treated at the Ellis Fischel State Cancer Hospital (1940–1971) for Hodgkin's disease and other malignant lymphomas. The institution is a referral center and has admitted 40,610 patients during the same period. About two-thirds of the patients had malignant disease documented. Very few pediatric cases are admitted and about 6–8 per cent of the cancer cases in the State of Missouri are seen at this hospital.

Of the 591 patients, 64 patients were excluded because the original diagnosis could not be confirmed in 37, and the diagnosis was based on outside reports only in 27.

A pathologist (J.M.H.) with special interest in malignant lymphomas has reviewed all the original slides and confirmed the diagnosis in 448 patients (in 21 patients the original diagnosis of Hodgkin's disease was changed to other types of lymphoma). In addition, slides of 79 patients were not available for review, but they are included in this study because the diagnoses of Hodgkin's disease or lymphoma made by outside pathologists were previously confirmed by pathologists at this hospital. Thus this report concerns itself with the clinical courses of 527 patients (163 with Hodgkin's disease, and 364 with other malignant lymphomas).

There were 99 males and 64 females with Hodgkin's disease (M:F = 1.5:1). The age range was 4 to 81 years (median = 40, mean = 43.5). There were 220 males and 144 females with other lymphomas. The male to female sex ratio was also 1.5:1. The age range was 4 to 88 years (median = 62, mean = 58.5). Figure 1 shows the age and sex distribution by 5 year intervals. In our series, as in others, the non-Hodgkin's lymphomas appeared mainly in older patients.

All the Hodgkin's lesions were reclassified

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From the Cancer Research Center, the Departments of Surgery and Pathology of the Ellis Fischel State Cancer Hospital and the Department of Surgery, University of Missouri Medical School, Columbia, Missouri.
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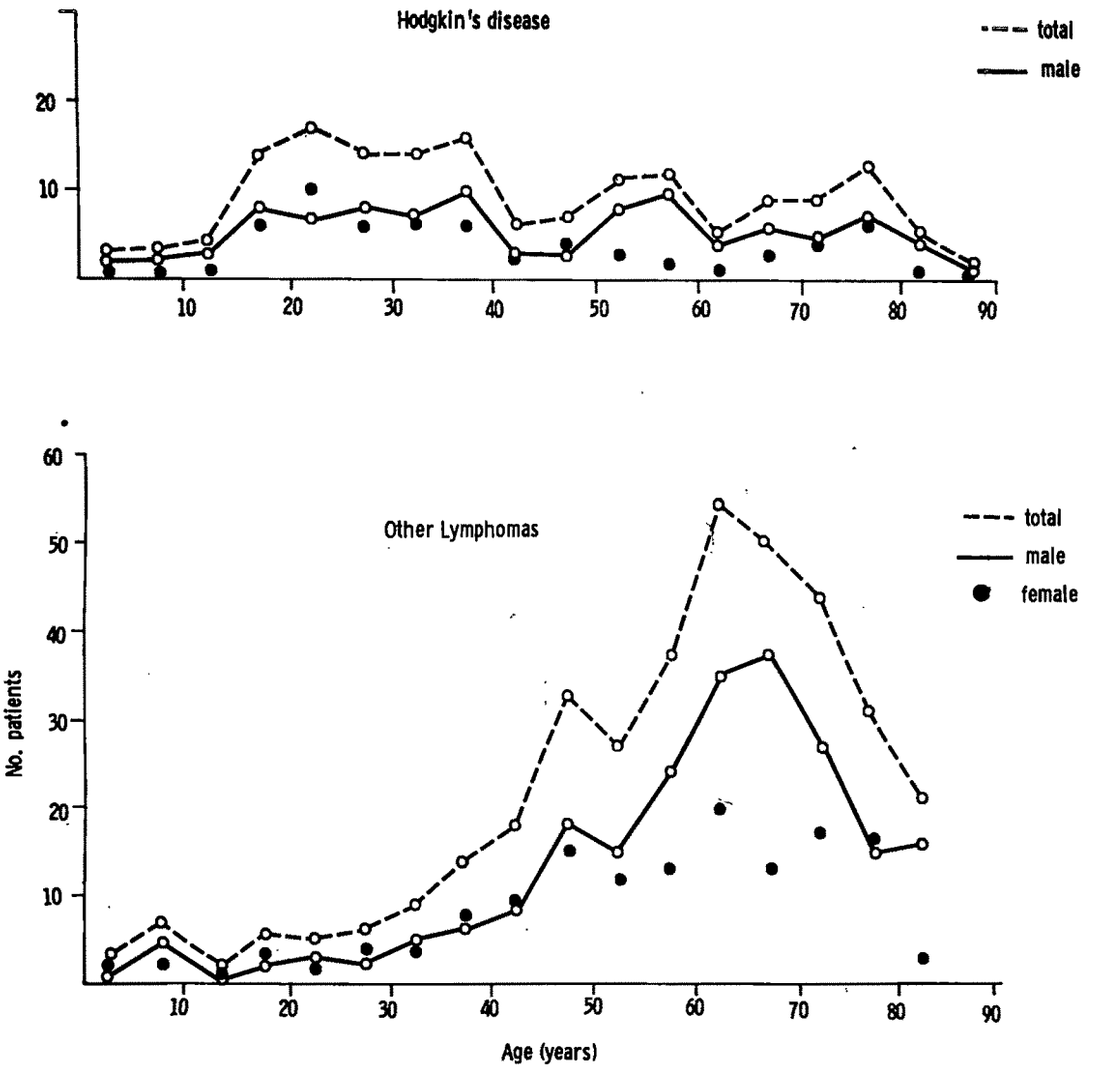


Fig. 1. Age and sex distribution of 163 cases of Hodgkin's disease and 364 cases of other lymphomas.

according to the Luke's proposal, modified and recommended at the 1965 Rye Conference.[3] Among our 163 cases, there were 28 of nodular sclerosis (17 per cent), 43 of lymphocytic predominance (26 per cent), 33 of mixed cellularity (20 per cent), 30 of lymphocytic depletion (19 per cent), and 29 patients whose slides were inadequate for classification (18 per cent). The non-Hodgkin's lymphomas were classified according to the terminology of Rappaport.[5] The distribution of our cases is presented in Table 1.

More than 200 clinicopathologic factors were abstracted from patient records, including details of radiotherapy and chemotherapy. The survival data presented are age-adjusted and calculated from the time of tissue diagnosis by the life-table method. All cases were classified into clinical stages according to the Rye classification[7] (except hepatomegaly as such was included in Stage IV). The distribution of the clinical stages and of the year of admission to Ellis Fischel State Cancer Hospital is presented in Figure 2.

TABLE I

DISTRIBUTION OF NON-HODGKIN'S LYMPHOMA

(Based on the Terminology of Rappaport, 1966)[5]

Old Diagnosis	No. of Patients	Lymphocytic		Histiocytic		Mixed Cellular	Undifferentiated	Unclassified
		WD*	PD*	WD*	PD*			
Reticulum cell sarcoma	121	12	19	21	20	12	22	15
Lymphocytic lymphoma	138	54	29	12	6	11	10	16
Lymphoblastic lymphoma	61	13	23	5	4	3	7	6
Giant follicular lymphoma	23	14	4	1	1	2	—	1
Hodgkin's disease	21	5	6	1	3	4	1	1
No. of patients	364	98	81	40	34	32	40	39
Per cent of total patients	100	27	22	11	9	9	11	11
Survial								
5 year	30%	46%	21%	18%	18%	24%		38%
10 year	14%	16%	13%	0	11%	10%		28%

* WD = well differentiated; PD = poorly differentiated.

Since this is a retrospective study, the modern techniques of staging were used rarely in the pretreatment studies (since 1965 only 10 patients have had abdominal exploration). The basic work-up consisted of complete blood cell counts, urinalysis, blood typing, chest roentgenography and electrocardiography. As listed in Table II, lymphangiography and radioisotope liver scanning were used in less than 10 per cent of the patients. From 30 to 70 per cent had gastrointestinal roentgenologic study and intravenous pyelography. Bone marrow biopsy—the majority was done by needle

TABLE II

ADDITIONAL PRETHERAPY SPECIAL PROCEDURES

	Hodgkin's Disease		Other Lymphomas	
	No.	Per Cent	No.	Per Cent
Lymphangiography (since 1962)	16 (6)*	10	22 (13)*	6
Liver scanning (since 1965)	10	6	11	3
Intravenous pyelography	107 (21)	66	251 (56)	69
Gastrointestinal roentgenology	51 (2)	31	188 (41)	52
Bone marrow study	78 (2)	49	182 (37)	50
Operation for staging (since 1969)	9	6	1	—
Operation for diagnosis	6	4	80	22
Celiotomy	4		54	
Radical mastectomy	1		4	
Lymph node dissection	1		5	
Wide excision	—		6	
Other	—		11	
Total Patients	163		364	

* Parentheses indicate numbers of patients with abnormal tests.

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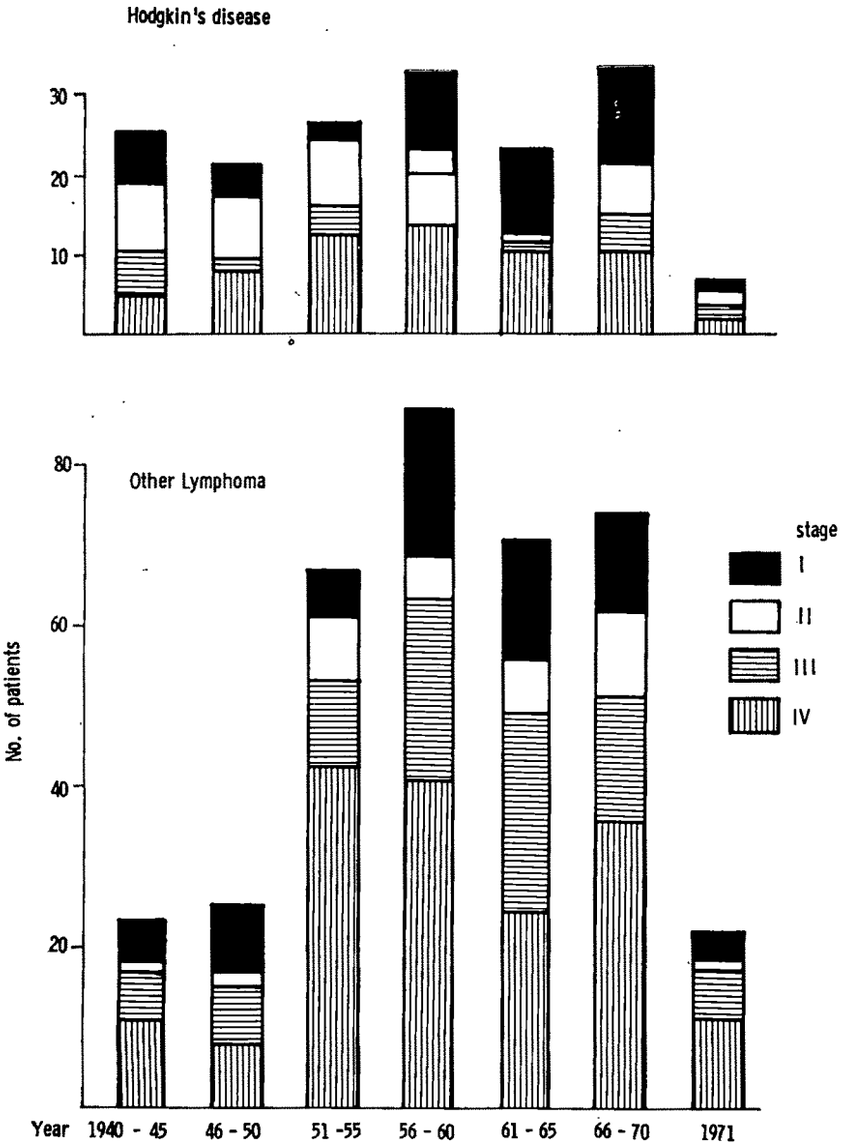


Fig. 2. Distribution of clinical stages and years of admission.

aspiration—was obtained in approximately 50 per cent of the patients. It is important to point out that in about 22 per cent of the cases with non-Hodgkin's lymphoma, major operations were involved in the diagnosis because peripheral lymphadenopathy was not obvious.

Factors Affecting Survival Rates

A. Age and Sex

Our over-all survival rates were similar for the patients with Hodgkin's disease and those with other lymphomas (age-adjusted 5 year survival=28 per cent, 10 year=16 per cent). In both groups, females have had a better survival curve (Fig. 3), but statistically this is not significant ($p>0.05$). In both groups, patients who belonged to the age group of 21 to 40 years have had the best survival rate (Fig. 4), and this difference is highly significant ($p<0.01$).

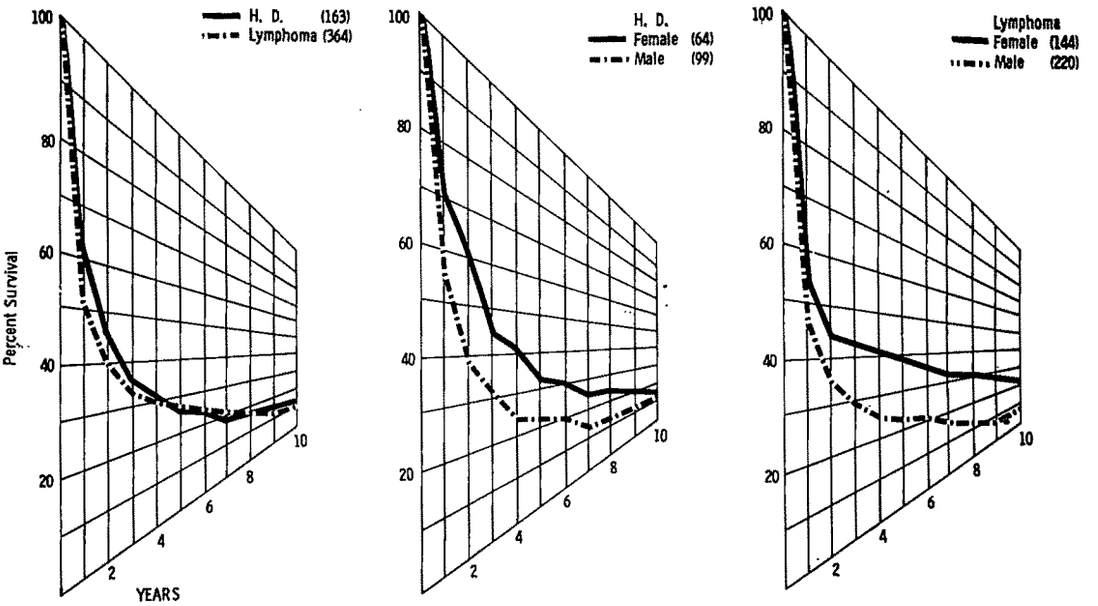


FIG. 3. Survival curves according to diagnosis and sex.

B. CLINICAL STAGE

In both groups, Stages I and II yielded better survival curves than Stages III and IV (the latter 2 groups had a very similar prognosis, especially those with Hodgkin's disease; Fig. 5). We found that the survival curves of patients with Stages I_2 (disease limited to 2 adjacent lymph node

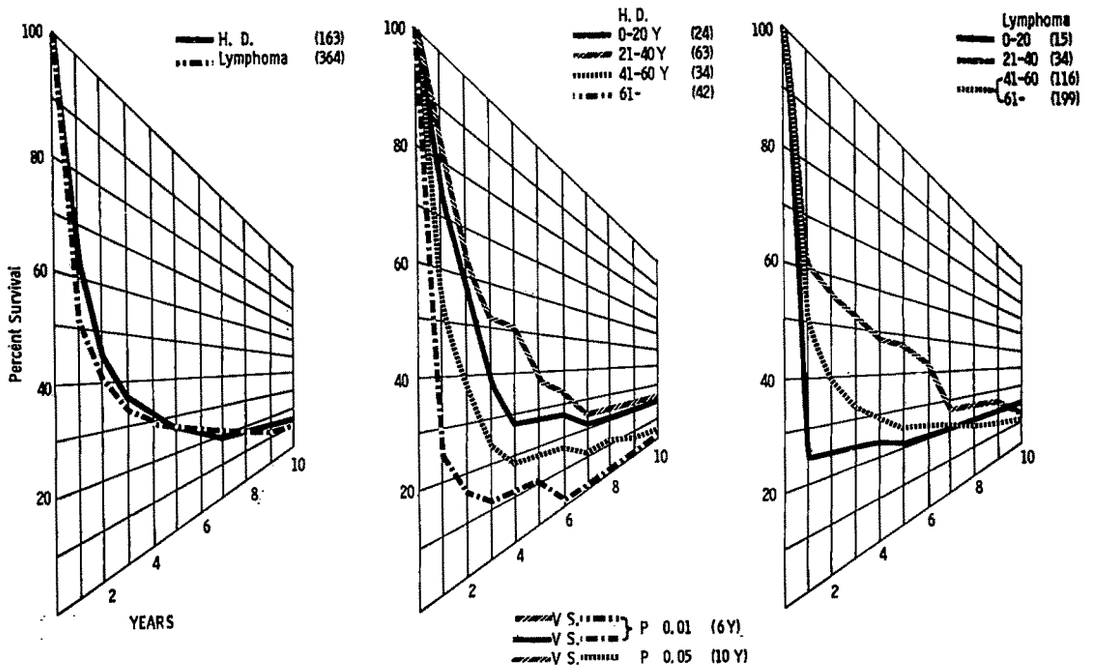


FIG. 4. Survival curves according to diagnosis and age.

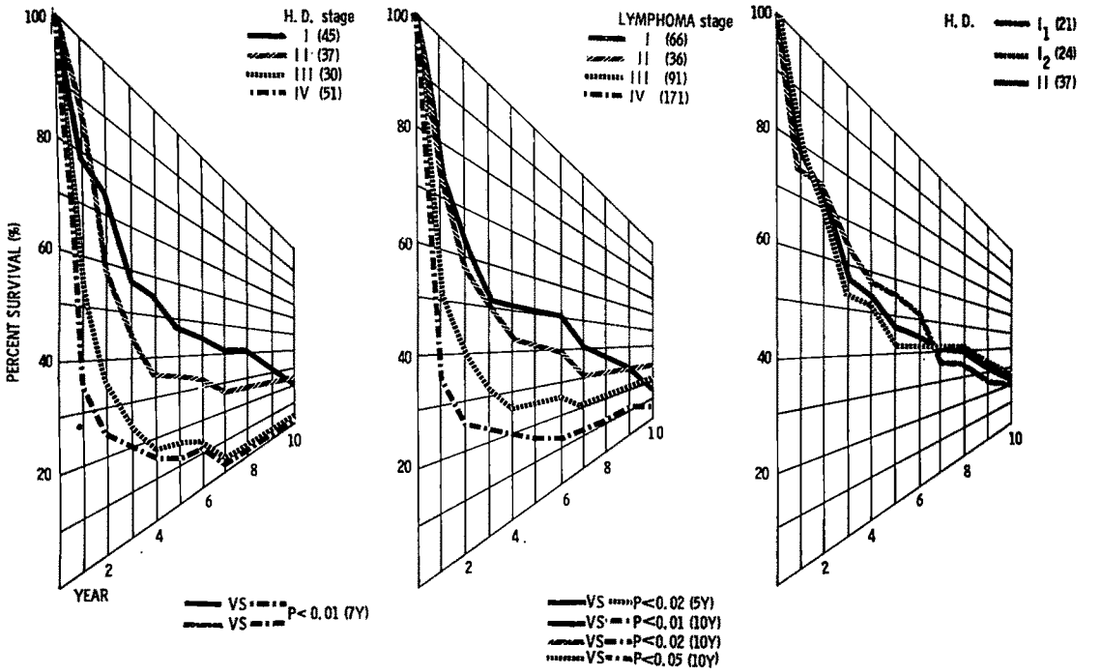


Fig. 5. Survival curves according to clinical Stage (I, II, III, IV, and I_1, I_2).

groups) and II (disease involving 2 non-adjacent, or more than 2 lymph node groups) were very close. This agrees with the recommendation of Carbone *et al.*[2] that the old Rye Stage I_2 should be combined with Stage II.

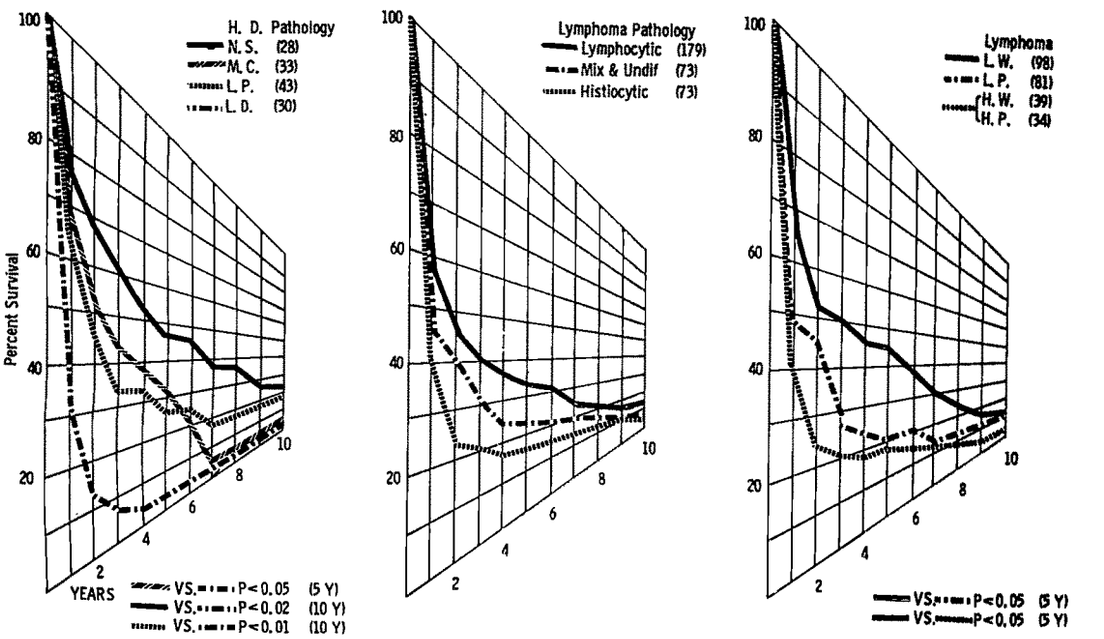


Fig. 6. Survival curves according to pathologic classifications.

TABLE III

HODGKIN'S DISEASE SURVIVAL *vs.* PATHOLOGY SUBTYPE

		LP	NS	MC	LD	Total
Pt. No.	Butler[1]	9–63	14–149	28–97	5–68	1,220
	EFSCH	43	28	33	30	163
5 year	Butler	50–88%	44–72%	3–58%	0–38%	26–57%
	EFSCH	26%	46%	34%	5%	28%
10 year	Butler	44–69%	25–53%	14–37%	4–20%	22–51%
	EFSCH	20%	20%	7%	5%	16%

EFSCH = Ellis Fischel State Cancer Hospital.
LP = lymphocytic predominance; NS = nodular sclerosis; MC = mixed cellularity; LD = lymphocytic depletion.

C. PATHOLOGIC CLASSIFICATIONS

In patients with Hodgkin's disease, our series showed that those with nodular sclerosis had the best prognosis and those with lymphocytic depletion, the poorest (Fig. 6). Our results are comparable to the data of 7 other series as summarized by Butler,[1] except for the subtype of lymphocytic predominance (Table III). For patients with non-Hodgkin's lymphomas, the difference between the various histologic types is not so significant, but well differentiated lymphocytic types had the best prognosis (Fig. 6; Table I). Very few reports have studied the prognostic significance of non-Hodgkin's histologic subtypes classified according to the terminology of Rappaport.[5] In the large series of lymphosarcomas as reported by Rosenberg *et al.*:[6] the over-all 5 year survival rate was 28 per cent; for lymphosarcoma it was 27 per cent; and for reticulum cell sarcoma, it was 23 per cent. The survival figures for our series are as follows: over-all—30 per cent 5 years, 14 per cent 10 years; lymphocytic group—35 per cent 5 years, 15 per cent 10 years; and histiocytic group—18 per cent 5 years, 6 per cent 10 years.

D. DECADE OF ADMISSION AND TYPES OF THERAPY

About 31 per cent of those with Hodgkin's disease and 24 per cent of those with other lymphomas had some radiotherapy before they were admitted to our hospital. Figure 7 shows that the prognosis of patients with Hodgkin's disease admitted since 1960 is much better than those admitted before, and the prognosis of patients who received both radiotherapy and chemotherapy is better than of those who received either treatment alone. Figure 8 shows that the proportion of Hodgkin's disease patients receiving radiotherapy and chemotherapy has increased since 1960. Also, it shows that the majority (76 per cent) of those patients with the diagnosis of lymphocytic predominance were admitted before 1960, contrasted with only 46 per cent of those with nodular sclerosis ($p < 0.02$). This might explain the poor survival result of our patients with the diagnosis of lymphocytic predominance.

For the patients with other lymphomas, there seems to be little difference in prognosis between decades of admission or types of therapy (Fig. 9). (Eleven of the 36 patients who received neither radiotherapy nor chemotherapy had surgical treatment [6 of the 11 lived longer than 10 years]. Four patients had limited excision and 7 had radical surgical removal.) However, those patients who had several courses of radiotherapy actually fared better. It is unclear whether or not this is artificial because those who survived longer might be patients who could receive more courses of radiotherapy. Also, the equipment, philosophy and technique of radiotherapy have changed over the years (Table IV): more patients are receiving

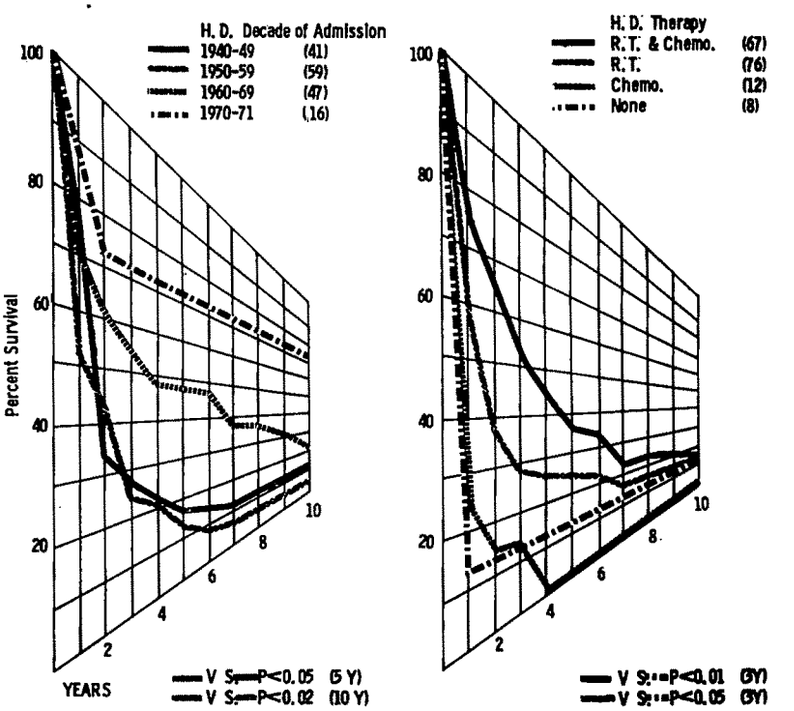


Fig. 7. Survival curves according to decades of admission and types of therapy (163 cases of Hodgkin's disease).

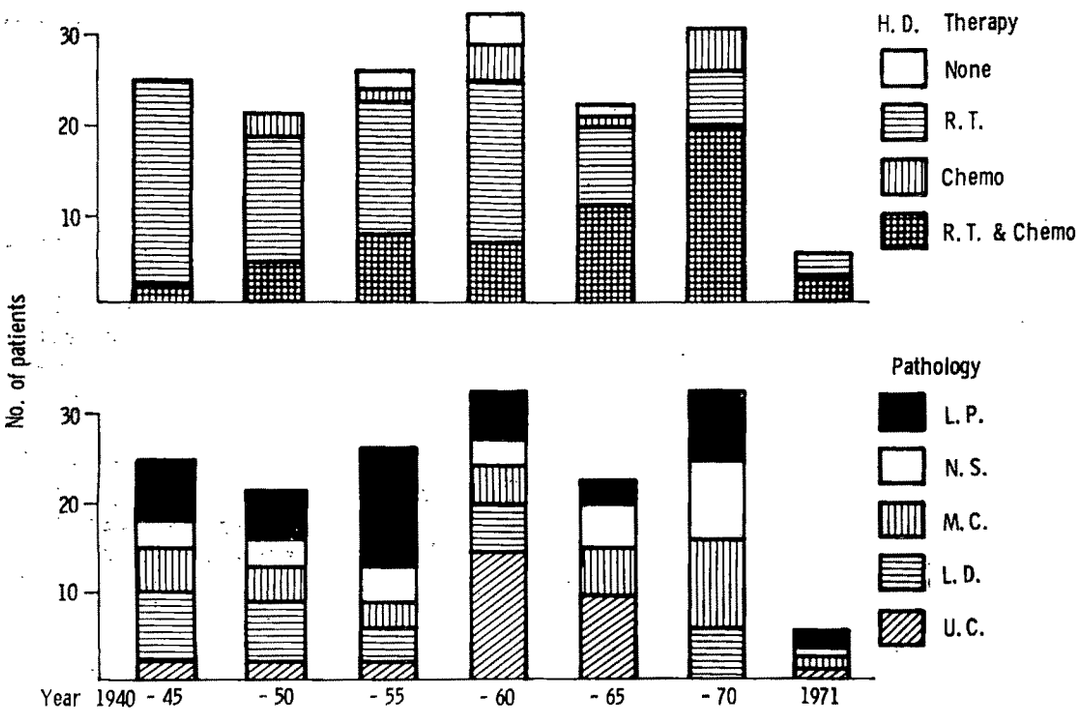


Fig. 8. Distribution of types of therapy, pathology subtypes and years of admission.

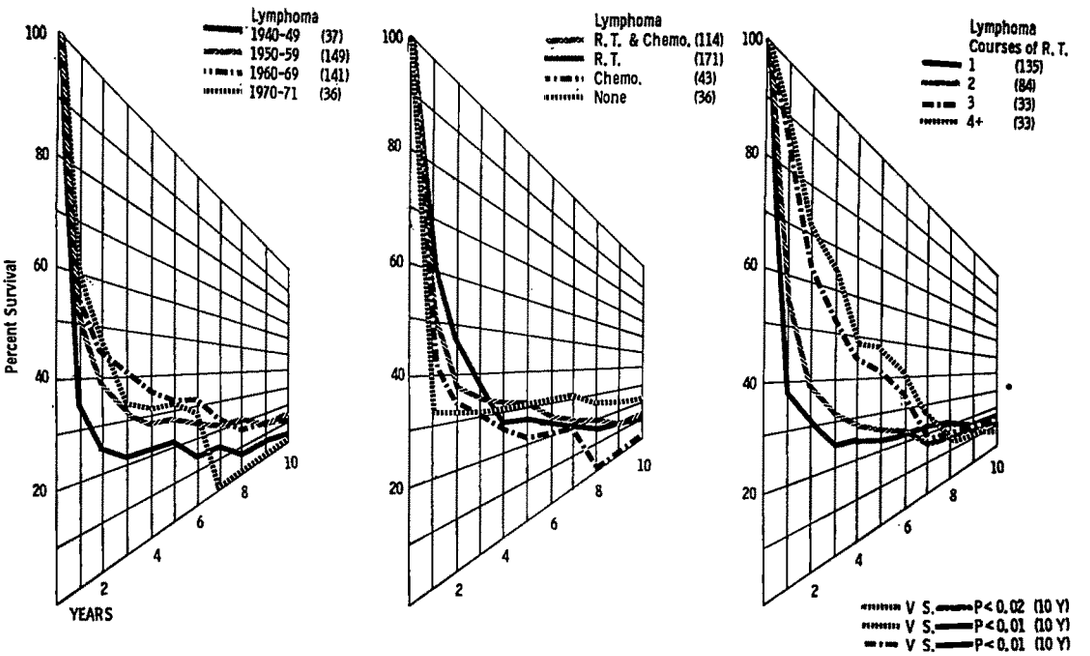


FIG. 9. Survival curves according to decades of admission, types of therapy and courses of radiotherapy (364 cases of other lymphomas).

TABLE IV

ANALYSIS OF FIRST RADIOTHERAPY GIVEN AT EFSCH

Year	Hodgkin's Disease					Other Lymphomas				
	No. of Patients	Radiation Therapy to Next Lymph Node		Given Dose (×100 r)*		No. of Patients	Radiation Therapy to Next Lymph Node		Given Dose (×100 r)*	
		No.	Per Cent	Range	Mean		No.	Per Cent	Range	Mean
1940–1945	20	2	10	10–27	18.7	15	—	—	10–30	19.4
1946–1950	16	1	6	12–40	26.8	11	—	—	10–33	25.3
1951–1955	22	3	14	10–50	26.9	42	—	—	10–52	25.2
1956–1960	20	3	15	10–28	20.1	58	—	—	10–60	24.5
1961–1965	17	5	29	11–50	35.1	27	5	18	10–42	25.3
1966–1970	21	7	33	10–50	37.4	40	9	23	10–68	39.7
1971	6	3	50	31–44	39.2	9	3	33	19–54	38.8
	122	24	20			202	17	8		

* Listed dose is highest dose given to an area, excluding total body radiation and incomplete therapy. Radiation therapy machine used: 1940–1950, 200 kv. and 218 kv.; 1950–1957, majority of the patients were treated with 250 kv.; since 1957, most were treated with cobalt 60 apparatus.

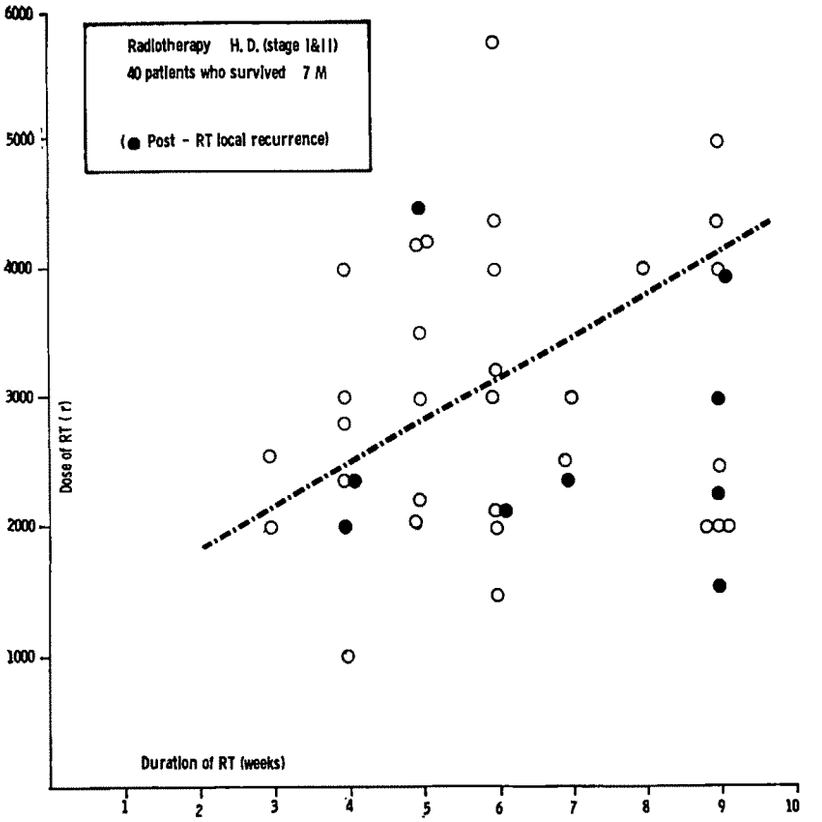


Fig. 10. Post-radiotherapy local recurrence *vs.* doses given and duration of therapy.

radiotherapy to adjacent lymph node areas (extended therapy), and the doses given have been increased. We attempted to analyze the relationship of local recurrence of lesions to doses given and duration of therapy for patients (Stages I and II) who received their first course of radiotherapy at our hospital. Figure 10 suggests that such a relationship might exist in the 40 patients with early Hodgkin's disease who survived longer than 6 months. No relationship was evident for patients with other lymphomas.

SUMMARY

This is a retrospective and all-inclusive study of 163 patients with Hodgkin's disease and 364 patients with other lymphomas who were admitted to a state cancer hospital from 1940 to 1971.

All the histologic diagnoses were confirmed and the cases were reclassified according to the Rye system for Hodgkin's disease and the Rappaport classification for non-Hodgkin's lymphomas.

Age-adjusted survival data are presented according to age, sex, clinical stage, pathologic subtype, decade of admission, and type of therapy.

Similarities and differences of the clinical courses of patients with Hodgkin's disease and other malignant lymphomas are discussed.

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A METHOD FOR THE CALCULATION OF DOSE IN THE RADIATION TREATMENT OF HODGKIN'S DISEASE[1]

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THE calculation of dose at depth for large, irregularly shaped treatment fields, such as mantle fields in the radiation treatment of Hodgkin's disease, is complex and is usually accomplished by approximations based upon, or corroborated by, measurements in phantoms.[21,25,26] The validity of an approximation is limited to the type of radiation machine, the points chosen for calculation, and other parameters such as field shape used during measurement. A general calculative method described here utilizes standard tabular data together with a few measurements on the therapy machine. The dose is separated into primary and scatter contributions, as has been described by Clarkson,[3,16] with allowances for the variation of exposure across the field and non-nominal source-skin distance (SSD) in parts of the field. A computer method embodying the same principles has been in use at the Princess Margaret Hospital, Toronto.[5] The method described here can be used to calculate the dose at any point in the patient within or outside the useful beam except near the edges of the field. It may be considered a standard of comparison for approximation methods without further experimental verification.

These discussions of calculative methods, considerations of dose to the spinal cord, the gonads, and between adjacent fields, and the construction of lung blocks were presented at a Hodgkin's Disease Dosimetry Workshop on June 26, 1969, at Chicago. The workshop was sponsored by the Cooperative Hodgkin's Disease Clinical Trial Steering Committee and conducted through the American Association of Physicists in Medicine by the Radiological Physics Center (RPC) and a task group of the Scientific Committee. The instructors and collaborators at the workshop appear as authors here, and this paper is intended to present the essentials of the discussions at the workshop.

Another method of dose calculation utilizing the tissue maximum ratio (TMR) definition of the dose at depth has been developed at the Memorial Hospital in New York.[14] This method is designed to be independent of energy and is in use at a number of institutions; however, it will not be presented in the discussions here.

CONSIDERATIONS IN CALCULATION

THE PROBLEM

In the treatment of Hodgkin's disease, large fields with outside borders of up to

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[11] Thomas Jefferson University Hospital, Philadelphia, Pennsylvania.

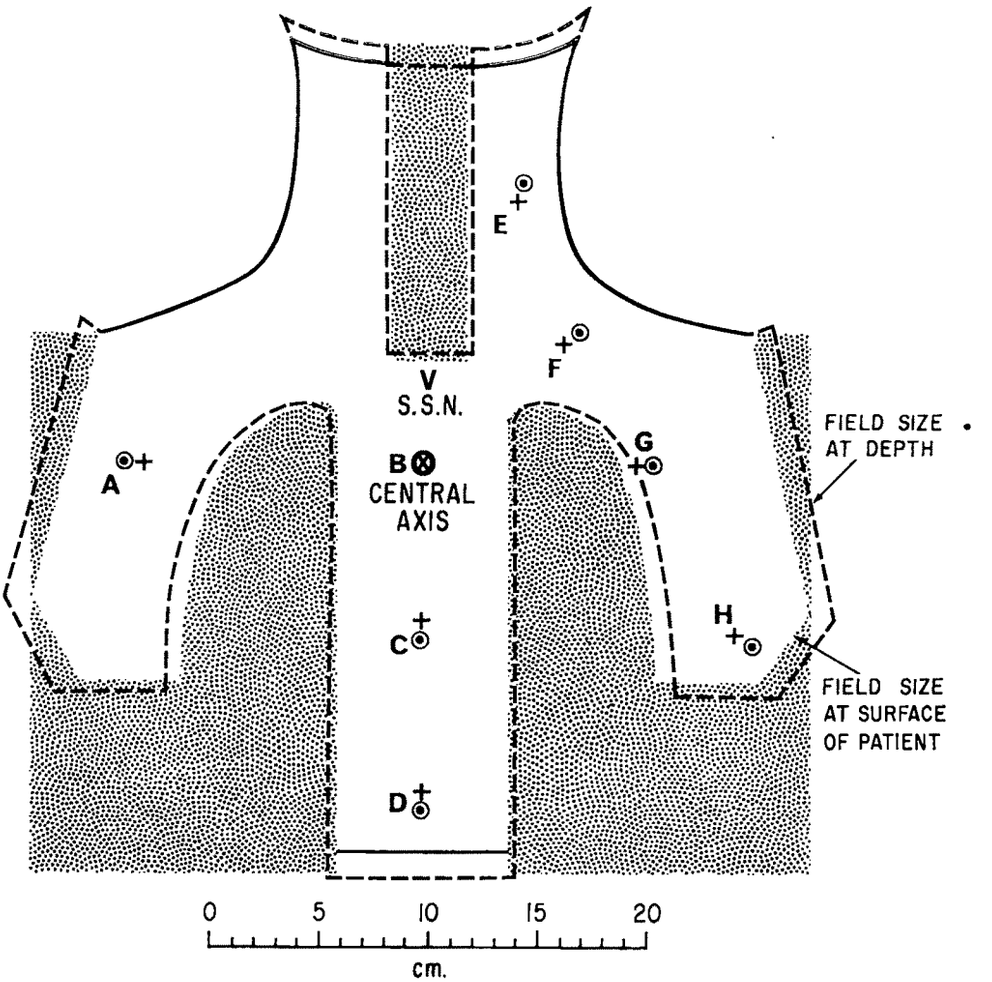


FIG. 1. Typical mantle field for radiation treatment of the neck and thorax. + = positions on surface of patient; ⊙ = the projection at mid-depth.

40×40 cm. are blocked to shield regions where the radiation is not desired, such as the lungs. The resulting treatment field will differ in shape from patient to patient; thus, it is not practical to have isodose curves available for each field shape and patient contour. An example in Figure 1 shows the outline of a field and a number of points chosen for calculation. A cross-sectional view of the same treatment plan which includes the central axis is shown in Figure 2. The departure from nominal SSD (g), relating to a point of calculation (A), at depth (d), is illustrated. For treatments of this type, high energy photon radiations usually are used, including cobalt 60 gamma rays and 2, 4, 6, or 8 MV roentgen rays, with SSD of 80 to 150 cm. With higher energy photons, there is danger of underdosing superficial regions in which electronic build-up has not been achieved, and some clinicians question the use of 6 and 8 MV roentgen rays for this reason. This danger may be more apparent than real, since with 8 MV roentgen rays the dose at 0.5 cm. depth is 90% of the maximum with a 30×30 cm. field, and 80% of maximum with a 10×10 cm. field.[23] With 6 MV roentgen rays, the dose at 0.5 cm. depth is 92% of the maximum with a

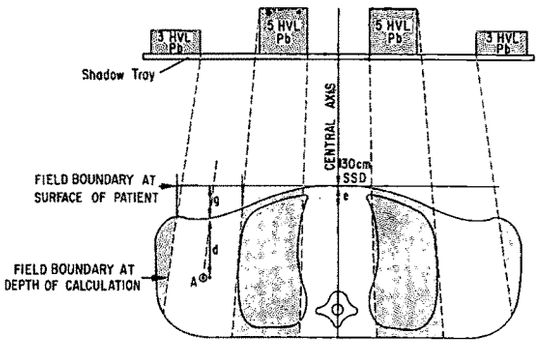


FIG. 2. Cross section through the patient in the axillary region at the level of the point of calculation, A.

25×25 cm. field and 86% of the maximum with a 10×10 cm. field.[24]

OFF-AXIS DIMINUTION OF THE BEAM

With large, irregularly shaped fields, it is necessary to take account of beam characteristics, just as with smaller fields of regular shape. With the latter, the off-axis diminution of the beam is implicit in the isodose curves; for the calculation of dose to the points in an irregular field for which isodose curves do not exist, however, the diminution across the beam must be allowed for explicitly. In Table 1, some typical beam profiles in air are shown for large fields, indicating that points off the central axis in a cobalt 60 beam may have an exposure of 8 or 9% less than the center. As is shown in the third column for cobalt 60, this effect can be diminished by utilizing the central part of a larger field with beam definition by secondary blocking, or alternatively by using a compensator to flatten the field, as is illustrated for 6 MV roentgen rays. Off-axis diminution may be measured in air with a detector having a wall of sufficient thickness to provide electronic equilibrium. Measurements across the unblocked field at the treatment distance on perpendicular axes and diagonals are usually sufficient. If the shadow tray is in place during the measurements, oblique attenuation near the edges of the field is taken into account.

NON-NOMINAL SOURCE-SKIN DISTANCE

The variation of SSD within the field of treatment is a source of error in the calculation considered. If the nominal SSD is 130 cm. and a portion of the skin is 4 cm. more distant, then an error of about 6% is introduced if the patient is considered flat at 130 cm.

INFLUENCE OF COLLIMATORS AND BLOCKING

The setting of the primary collimators influences the exposure rate significantly,

TABLE I

BEAM PROFILE IN AIR, RELATIVE TO THE CENTRAL AXIS FOR LARGE FIELDS*

Distance from Side of Field (cm.)	Co^{60}	Co^{60}	2 MV Roentgen Rays	6 MV Roentgen Rays
	100 cm. SSD 35×35 cm. Trimmers 65 cm.	130 cm. SSD 53×52 cm. Blocked to 34×34 cm.	150 cm. TSD 35×35 cm.	160 cm. TSD 40×40 cm.
(Center of field)	1.00	1.00	1.00	1.00
12	.99	1.00	1.00	1.00
10	.99	.99	.99	1.00
8	.98	.98	.98	1.00
6	.97	.98	.97	1.00
5	.96	.97	.96	1.00
4	.95	.97	.95	1.00
3	.94	.96	.94	1.00
2	.92	.96	.92	1.00
1	.91	.95	.91	—

* Measurements were in air on particular machines. The results are not applicable generally to other similar machines.

but the presence of secondary blocking, such as for the lungs, may increase or decrease the exposure rate slightly—usually less than 1%. This occurs because of the large contribution of scatter radiation from the collimating parts near the source and the relatively small contribution of scatter from secondary collimators at a distance from the source. Therefore, it is sufficient that the exposure rate in air or absorbed dose rate in free space[16] from a machine be known or calculated with the primary collimators as they are set in treatment prior to the addition of secondary blocking.

GENERAL METHOD

The general method consists of a summation at each point of interest of the primary and scattered radiation with allowance for the off-axis diminution and non-nominal SSD. The primary radiation to a point of interest is calculated using the tissue-air ratio (TAR) for zero field size, and the scatter radiation is calculated from scatter-air ratios (SAR). The TAR is defined as the ratio of the absorbed dose at a given point in a phantom to the absorbed dose which would be measured at the same point in free air within a volume of the phantom material just large enough to provide the maximum electronic buildup at the point of measurement.[15] The SAR is defined as the difference between the TAR for a given field and the TAR at the same depth for zero field size.[13] The data for these calculations are given in Table II.

The absorbed dose at an arbitrary point

TABLE IIA

TISSUE-AIR RATIOS AND SCATTER-AIR RATIOS

A. Cobalt 60

Depth	Tissue-Air Ratio*		Scatter-Air Ratios for Field Radius†							
(cm.)	0 cm.²	100 cm.²	2 cm.	4 cm.	6 cm.	8 cm.	10 cm.	15 cm.	20 cm.	25 cm.
0.5	1.000	1.036	.014	.026	.037	.048	.058	.076	.085	.089
1	.965	1.028	.025	.048	.066	.078	.089	.107	.118	.123
2	.905	1.002	.045	.080	.102	.116	.127	.149	.160	.167
3	.845	.971	.061	.103	.130	.147	.161	.184	.198	.205
4	.792	.938	.071	.121	.151	.170	.186	.210	.228	.239
5	.742	.902	.076	.134	.166	.189	.206	.235	.255	.266
6	.694	.864	.080	.141	.176	.201	.219	.252	.272	.284
7	.650	.825	.081	.143	.181	.209	.229	.267	.290	.304
8	.608	.785	.080	.142	.185	.214	.236	.278	.301	.315
9	.570	.746	.078	.140	.183	.216	.240	.284	.312	.327
10	.534	.707	.075	.136	.181	.215	.242	.288	.318	.336
11	.501	.671	.071	.132	.178	.213	.241	.289	.322	.339
12	.469	.635	.069	.128	.174	.210	.239	.290	.324	.342
13	.440	.602	.066	.124	.170	.207	.237	.290	.325	.345
14	.412	.570	.063	.120	.168	.204	.235	.288	.326	.347
15	.386	.539	.060	.116	.162	.200	.231	.286	.325	.347
16	.361	.511	.058	.112	.157	.196	.227	.283	.322	.346
17	.338	.484	.056	.108	.153	.191	.223	.279	.318	.343
18	.317	.459	.054	.104	.148	.186	.218	.275	.313	.339
19	.297	.433	.052	.101	.144	.181	.213	.270	.309	.335
20	.278	.409	.049	.097	.139	.176	.207	.265	.305	.329

* *Brit. J. Radiol.*, 1968.
† Gupta and Cunningham, 1966.

TABLE IIB

TISSUE-AIR RATIOS AND SCATTER-AIR RATIOS

B. 4 MV Roentgen Rays: Varian Clinac-4 (Lead Flatness Filter)

Depth	Tissue-Air Ratio		Scatter-Air Ratios for Field Radius							
(cm.)	0 cm.²	100 cm.²	2 cm.	4 cm.	6 cm.	8 cm.	10 cm.	15 cm.	20 cm.*	25 cm.*
1.2	1.000	1.037	.013	.026	.039	.052	.062	.073	.077	.079
2.0	.952	1.021	.035	.055	.073	.088	.098	.110	.115	.118
3.0	.899	.998	.048	.081	.102	.118	.130	.143	.150	.154
4.0	.847	.966	.058	.097	.125	.145	.157	.174	.188	.195
5.0	.799	.933	.063	.110	.141	.165	.179	.200	.214	.222
6.0	.753	.900	.067	.119	.155	.181	.196	.220	.237	.246
7.0	.710	.866	.068	.125	.163	.193	.211	.237	.257	.268
8.0	.670	.832	.069	.128	.170	.201	.222	.252	.272	.283
9.0	.632	.800	.069	.131	.174	.207	.230	.263	.283	.296
10.0	.598	.765	.068	.132	.177	.210	.236	.271	.291	.303
11.0	.564	.731	.067	.131	.178	.213	.240	.278	.300	.315
12.0	.529	.698	.066	.130	.178	.215	.242	.283	.308	.318
13.0	.500	.666	.065	.128	.177	.214	.243	.288	.314	.325
14.0	.471	.636	.063	.125	.175	.212	.243	.289	.316	.330
15.0	.444	.605	.062	.122	.171	.210	.241	.290	.316	.330
16.0	.419	.576	.060	.118	.168	.206	.239	.289	.316	.325
17.0	.395	.549	.059	.114	.163	.202	.235	.287	.314	.323
18.0	.373	.521	.057	.110	.159	.197	.230	.284	.312	.320
19.0	.351	.496	.056	.107	.154	.193	.226	.281	.310	.318
20.0	.331	.473	.054	.104	.150	.188	.221	.276	.306	.314

* Extrapolated data.

Notes: (1) Table by Mary Peterson of Rosewood General Hospital and Robert Golden of the AAPM Radiological Physics Center from measurements at Wadley Institute, Dallas, Texas.

(2) This machine produced a depth dose of 60.8 per cent at 10 cm. depth for a 10×10 cm. field at 80 cm. target-skin distance and a tissue-maximum ratio of 0.738 at 10 cm. depth for a 10×10 cm. field at 80 cm. target-axis distance.

A, as shown in Figures 1 and 2, is calculated as follows:

Absorbed dose at point A =

[absorbed dose in phantom for calibration conditions]

× [transition to absorbed dose in a small mass of tissue for treatment field size]

× [transition to absorbed dose in a small mass of tissue at point A]

$$\times \left[\frac{\text{(absorbed dose due to primary radiation to point A in patient)} + \text{(absorbed dose due to scatter radiation to point A in patient)}}{\text{absorbed dose in a small mass of tissue at point A}} \right].$$

Symbolically, with the brackets having the same meaning as above, the absorbed dose

TABLE IIC

TISSUE-AIR RATIOS AND SCATTER-AIR RATIOS

C. 6 MV Roentgen Rays: Varian Clinac-6

Depth	Tissue-Air Ratio		Scatter-Air Ratios for Field Radius							
(cm.)	0 cm.²	100 cm.²	2 cm.	4 cm.	6 cm.	8 cm.	10 cm.	15 cm.	20 cm.	25 cm.
1.5	1.000	1.029	.010	.021	.031	.042	.051	.063	.069	.071
2	.997	1.027	.011	.021	.032	.043	.052	.064	.069	.071
3	.965	1.009	.016	.032	.047	.058	.067	.083	.089	.090
4	.926	.981	.020	.040	.057	.071	.082	.099	.108	.111
5	.885	.952	.024	.049	.071	.087	.100	.117	.126	.130
6	.843	.924	.030	.060	.085	.105	.118	.137	.147	.151
7	.802	.895	.035	.070	.098	.120	.134	.155	.166	.171
8	.761	.866	.040	.079	.111	.134	.149	.172	.184	.189
9	.722	.837	.043	.087	.121	.145	.162	.188	.200	.206
10	.687	.808	.046	.091	.127	.151	.170	.199	.212	.217
11	.655	.779	.047	.093	.131	.157	.178	.207	.221	.227
12	.624	.750	.047	.093	.133	.162	.184	.213	.228	.236
13	.596	.722	.047	.093	.133	.163	.185	.218	.235	.245
14	.567	.694	.047	.093	.134	.165	.187	.224	.243	.254
15	.540	.668	.047	.094	.136	.168	.191	.226	.247	.262
16	.513	.642	.048	.095	.137	.171	.193	.229	.252	.269
17	.488	.618	.048	.096	.138	.171	.194	.232	.256	.274
18	.464	.593	.048	.096	.137	.170	.194	.234	.259	.278
19	.443	.570	.048	.094	.134	.167	.192	.232	.259	.278
20	.422	.546	.047	.091	.130	.164	.189	.230	.258	.278

Notes: (1) Table by J. H. Cundiff and R. Golden of the AAPM Radiological Physics Center with the collaboration of L. H. Deiterman, verified on the 6 MV Varian Clinac X-ray machine at Scott and White Clinic, Temple, Texas.
(2) This machine produced a depth dose of 67.5 per cent at 10 cm. depth for a 10×10 cm. field at 100 cm. target-skin distance and a tissue-maximum ratio of 0.785 at 10 cm. depth for a 10×10 cm. field at 100 cm. target-axis distance.

at point A can be calculated for source-skin or isocentric techniques.

Fixed source-skin distance; calibration in phantom.

$$D_A = [D_c \times B]\left[\frac{1}{TAR)_e} \times G\right] \cdot \left[P \times \left(\frac{SSD + e}{SSD + g + d}\right)^2\right] \cdot [TAR)_d + S_d]. \quad (1)$$

Isocentric technique; calibration in phantom.

The rationale for an isocentric technique is the same.

$$D_A = [D_i \times B]\left[\frac{1}{TAR)_i} \times G\right] \cdot \left[P \times \left(\frac{SAD}{SPD}\right)^2\right] [TAR)_d + S_d]. \quad (2)$$

Fixed source-skin distance; cobalt 60 or 2 MV x-ray, calibration in air.

The rationale with in-air calibration is the same as for equation (1), except the factor, $TAR)_e$ is not required.

$$D_A = [D_a \times B][G] \cdot \left[P \times \left(\frac{SSD + e}{SSD + g + d}\right)^2\right] \cdot [TAR)_d + S_d]. \quad (3)$$

D_A = absorbed dose at arbitrary point A.

D_c = absorbed dose in phantom for same SSD as used in treatment at depth of dose maximum (measured at or corrected to this depth) for the calibration field size.

D_i = absorbed dose in phantom at depth of calibration at source-tumor distance (or SAD) for the calibration field size.

D_a = absorbed dose in small mass of tissue, just sufficient for electronic equilibrium, in-air at nominal SSD+e, for the calibration field size.

B = fractional transmission of gamma rays through tray supporting secondary blocking for field size utilized.

$TAR)_c$ = tissue-air ratio for the calibration field size at depth of dose maximum (this is the backscatter factor).

$TAR)_i$ = tissue-air ratio for the calibration field size at the depth of calibration.

G = relative field size dependence (measured in-air at the center of the large unblocked field to be employed; at calibration field size in-air, G is 1.00).

P = beam diminution off-axis in-air at the nominal SSD or SAD over the point to be calculated, for the large unblocked field; central axis is 1.00.

SSD = nominal source-skin distance for treatment with the irregular field.

e = depth of dose maximum.

g = vertical distance between skin surface over A and nominal SSD (beam vertical).

d = vertical depth, skin surface to A.

SAD = source-axis distance.

SPD = distance, source to point of calculation (such as point A).

$TAR)_d$ = tissue-air ratio at depth d for *zero field size.*

S_d = average scatter-air ratio for point A at depth d for the treatment field.

In a strict implementation of Equations (1), (2), and (3), the field size at the depth of calculation should be employed for scatter-air calculations, and the $TAR)_d$ for zero field size should be for the slant distance on the ray from the patient's surface to A. In practice, however, it is acceptable that the field size at the surface of the patient and also the vertical tissue depth for $TAR)_d$ be used in calculation. This recommendation leads to 2 errors which are almost mutually compensatory. The use of the field size at the nominal SSD instead of that at the depth of calculation can lead to an underestimation of dose by 1% or so, while utilizing the vertical depth instead of the slant depth overestimates the dose by about 0.5%. It is thus recommended that the field size at the nominal SSD and the vertical depth of tissue over a point of calculation be utilized.

The average scatter-air ratio (S_d) at a given point off-axis is calculated by summing the contributions from a number of sectors with equal angles, as shown in Figure 3. The scatter-air ratios for various circular field sizes for the depth (d) may be marked on a transparent ruler for direct reading. Different rulers must be prepared for each depth. Scatter-air ratios are independent of SSD, and the same tables may be used at different distances from the source. The sum of the contributions from all the sectors is divided by the number of sectors (36 in Fig. 3) to obtain the average.

Example of calculation at axilla for cobalt 60

Point A in Figure 2 and Figure 3.

SSD = 130 cm.

e = 0.5 cm.

D_c = absorbed dose at 130.5 cm. (10 × 10 cm. field at 130 cm.)

$TAR)_c$ = 1.036 (10 × 10 cm. field, 0.5 cm. depth)

B = 0.95

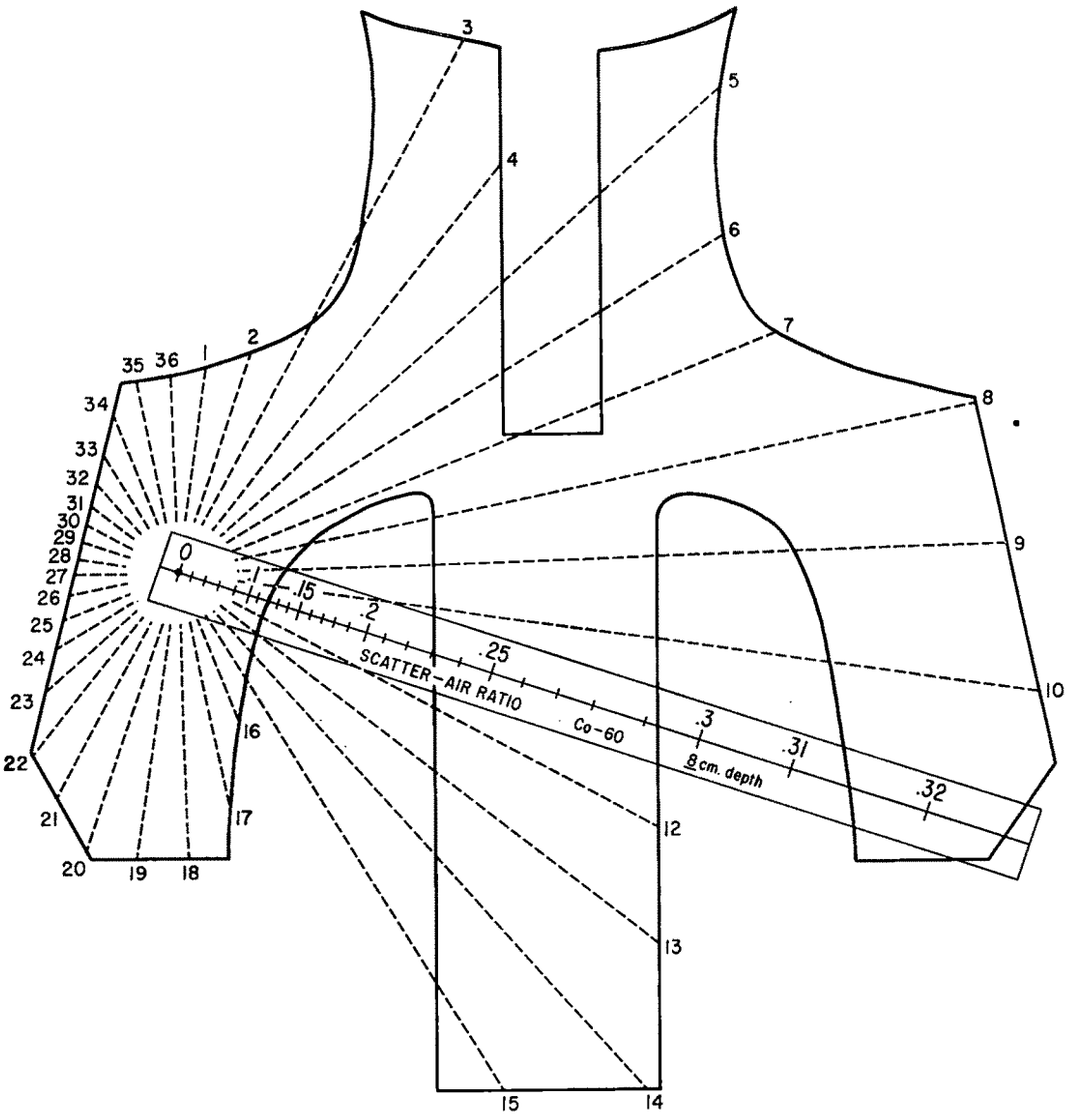


FIG. 3. The method of obtaining the average scatter-air ratio from equal sectors centering on point A. Regions under heavy blocking are considered as contributing no scatter.

$G = 1.05$ (36×36 cm. field at 130 cm. relative to a 10×10 cm. field at 130 cm.)
$P = 0.96$ (5 cm. inside field boundary defined by primary collimators)
$g = 4.0$ cm.
$d = 8.0$ cm.
$TAR)_d = 0.608$ (zero field size, 8 cm. depth)
$S_d = 0.200$ (from average scatter-air ratio calculation outlined in Table III)

From Equation (1):

$$D_A = [D_c \times 0.95]\left[\frac{1}{1.036} \times 1.05\right] \cdot \left[0.96 \times \left(\frac{130 + 0.5}{130 + 4.0 + 8.0}\right)^2\right] \cdot [0.608 + 0.200]$$

$$D_A = 0.631\ D.$$

TABLE III

CALCULATION OF AVERAGE SCATTER-AIR RATIO TO POINT A IN FIGURES 2 AND 3

Sector	Scatter-Air Ratio (SAR)					Net SAR
1	+.208					+.208
2	+.218					+.218
3	+.306	+.238	−.269			+.275
4	+.297					+.297
5	+.316	+.280	−.302			+.294
6	+.310	+.266	−.292			+.284
7	+.310	+.263	−.284			+.289
8	+.321	+.158	−.228			+.251
9	+.321	+.288	+.134	−.308	−.227	+.208
10	+.322	+.289	+.125	−.311	−.228	+.197
11	+.323	+.292	+.121	−.314	−.231	+.191
12	+.300	+.122	−.239			+.183
13	+.307	+.127	−.249			+.185
14	+.315	+.137	−.266			+.186
15	+.308	+.150	−.289			+.169
16	+.180					+.180
17	+.223					+.223
18	+.238					+.238
19	+.240					+.240
20	+.242					+.242
21	+.228					+.228
22	+.219					+.219
23	+.192					+.192
24	+.165					+.165
25	+.149					+.149
26	+.140					+.140
27	+.132					+.132
28	+.130					+.130
29	+.130					+.130
30	+.132					+.132
31	+.138					+.138
32	+.149					+.149
33	+.164					+.164
34	+.188					+.188
35	+.200	Average SAR $= \frac{7.216}{36} = .200$				+.200
36	+.202					+.202
					Total	+7.216

Comments on the calculation.

The above calculations are not valid near the edges of the open fields as defined by the secondary blocking, since the beam penumbra will reduce the dose there. At distances of 1.5 cm. and greater from the edges of the beam, the effects due to penumbra are usually small. If one wishes to calculate within the penumbra near the edges of the secondary blocking, it is possible to measure in-air across the field with the secondary blocks in place. An exaggerated off-axis correction factor (P) can be derived and applied. One would expect a lower accuracy in this region.

APPROXIMATE METHODS

Some institutions utilizing similar field shapes from patient to patient use an effective area for each point of calculation to choose an appropriate backscatter factor and per cent depth dose. The general method described above is useful in checking the validity of an equivalent area ap-

proximation. The best choice of effective area is that area which gives the same TAR as the general method. The equivalent area is πr^2, where r, the radius, is selected from Table II to give the scatter-air ratio calculated by the general method. In Table IV, the equivalent radii and areas are listed for the points noted in Figure 1.

As an aid in selecting equivalent areas for calculation, some institutions have evolved rules-of-thumb which are very helpful. The reader is cautioned against using rules-of-thumb unless he has checked their validity by the general method for his machine and his method of treatment.

COMPARISON OF CALCULATIONS AND MEASUREMENTS

The general method of calculation is proposed as a definitive method, not requiring further experimental verification. Accordingly, 3 approaches have been taken to challenge the calculative method: (1) uncertainties in the general method; (2) measurements in an idealized phantom; and (3) measurements in an anatomic phantom.

UNCERTAINTIES IN THE GENERAL METHOD

A summary of types of known uncertainties in the general calculative method, together with a measurement or estimate of each, appears in Table v. These entries are appropriate to points in the open parts of the field such as point A. The low density of lung beneath the lung blocks does not fully attenuate the scatter from distant parts of the open field, as indicated in Item 1 of this table. Item 2 arises because of the assumption in scatter-air tables that all parts of the field are at the same SSD; the general method allows for the effect of non-nominal SSD for the primary radiation but not for the scattered radiation. Item 3 is an estimate of the effect of the limited thickness of scattering media beneath or adjacent to such areas as the neck or axilla, which fail to provide full scatter to the point of calculation. Some transmission of primary radiation occurs through the lung blocks with subsequent scatter to points of calculation. Since lung blocks usually attenuate the primary beam to about 5% transmission, it is estimated that scattered radiation contributed by non-zero primary under shielding contributes on the order of 1% of the total absorbed dose at a point in the open field (Item 4). These uncertainties are estimates, or partial estimates, and they are added to obtain an over-all uncertainty of about $\pm 3\%$ in the correctness of the calculation. In this context, "uncertainty" does not have a rigorous definition, but it is likely that errors due to the above causes would fall within the stated range 95% of the time; if this is so, the standard error due to the above causes would be less than $\pm 2\%$.

TABLE IV

EQUIVALENT RADII AND AREAS FOR THE POINTS NOTED IN FIGURE 1 DERIVED BY THE GENERAL METHOD

Point	Equivalent Radius* (cm.)	Equivalent Area* ($cm.^2$)
A	7.00	154
B	9.19	265
C	8.43	223
D	5.76	104
E	5.20	85
F	8.00	201

* These values are applicable only to the example presented in Figure 1.

TABLE V

UNCERTAINTIES IN THE GENERAL METHOD

	Measured/ Calculated
Effect on scattered radiation of:	
1. Lesser density of lung beneath block	1.01
2. Non-nominal SSD	0.99–1.01
3. Limited phantom	0.98–1.00*
4. Transmission through blocks	1.01*
	1.00±0.03

* Estimated.

TABLE VI

COMPARISON OF THE GENERAL METHOD OF CALCULATION AND MEASUREMENTS

A. Idealized Phantom (Grant, 1970)

Point	Depth (cm.)	Dose Calculated/ Dose Measured
A	10.0	.98
B	10.0	1.00
C	10.0	1.00
D	10.0	.97
E	5.2	.98
F	0.5	1.00
G	10.0	1.00
H	10.0	.97
		Average 0.99±0.02

B. Anatomic Phantom (Grant, 1970)

Point	Dose Calculated/Dose Measured	
	Phantom inhomogeneities not considered	Phantom inhomogeneities considered
A	1.04±.02	1.02±.02
B	1.02±.01	1.00±.01
C	1.05±.03	1.03±.03
D	.96±.03	.95±.03
E	1.02±.01	1.02±.01
F	1.00±.01	.97±.01

MEASUREMENTS IN AN IDEALIZED PHANTOM

Measurements were made with a Farmer-Baldwin, 0.6 cc. ionization chamber and a Keithley 602 electrometer in a rectangular water tank utilizing cobalt 60 gamma rays and the field shape and points of measurement indicated in Figure 1. Thus, the entrance surface of the phantom was flat at the nominal SSD (100 cm.) and no inhomogeneities were present beneath the surface. Lung blocks of 5 cm. lead to shape the field were employed at a distance of 20 cm. from the water surface. The results shown in Table VIA are expressed as the ratio of dose calculated/dose measured.[12] The method of calculation was the general method described above. For point G, the off-axis correction factor was measured in air with the lung blocks in place, since the point is near the edge of the field. For the points considered, the average agreement between calculation and measurement in this idealized case was 1%. The standard error is estimated at 2%.

MEASUREMENTS IN AN ANATOMIC PHANTOM

An Alderson phantom loaded with lithium fluoride dosimeters was exposed in 6 experiments to cobalt 60 gamma rays utilizing the field shape and points of measurement indicated in Figure 1. The dose at mid-depth was compared with the dose calculated by the general method of calculation. The first column in Table VIB[12] is the ratio of the dose calculated to that measured, considering as muscle density the parts of the phantom exposed to the open radiation field; the second column corrects the scatter calculations for incursions of lung (at density 0.33) into the exposed area. This correction was necessary in this experiment because the Alderson phantom used had abnormally large lungs resulting in incomplete shielding of the lung area with lead. One should not need to make this correction for a clinical situation since the lung normally is completely shielded. Thus, the second column is a more correct comparison of the general calculative method and measurement. The experimental errors indicated are the standard deviations derived from variability of the data.

In the view of the authors, these lines of experiment and reasoning support the general method of calculation.

LUNG BLOCKS

POSITION

The support trays for lung blocks and other secondary blocking are usually located 15 cm. or more from the surface of the patient. The closer the blocks are to the patient, the less the penumbra cast by the edges of the blocks, but also the greater the surface dose due to secondary electrons ejected from the blocks and tray.[1] If the field size is large, the skin sparing characteristics of the beam will be reduced, even with a 15 cm. skin distance. For example, for cobalt 60 radiation through a plastic

tray, the skin dose is 45% of the subcutaneous dose at maximum for a field size of 12×12 cm. and a skin-to-tray distance of 15 cm.;[18] however, for a 30×30 cm. field, the skin dose is about 70% that at maximum.[27] The relative skin dose depends not only on field size and distance but also upon the material and type of shadow tray. For any given field size or skin-to-tray distance, a solid plastic tray gives the greatest dose to the skin. The use of plastic or metal trays in the form of an open mesh may improve skin sparing somewhat; however, in those instances where optimum skin sparing is desired, a material of intermediate atomic number may be placed on the side of the shadow tray nearest the patient. For a 30×30 cm. field at 15 cm. distance, the dose to the skin is reduced to about 50% of that at the maximum by the addition of copper, tin, or leaded glass on the underside of the shadow tray.[27]

CONSTRUCTION OF BLOCKS

The attenuation of the beam to about 5% is desired under the lung blocks. Generally 5 cm. of lead is used for this purpose, both for cobalt 60 gamma rays and 6 MV roentgen rays. A shape to shield the lung may be achieved by building with general blocks, by cutting from a lead slab for individual patients, or by building the proper shape from lead shot or low melting alloy.

Several techniques exist for determining the shape of blocks for individual patients. Meurk[22] utilizes a pantograph and the chest roentgenogram to produce a template for the cutting of lead blocks (with a 4 TPI skiptooth blade on a bandsaw). An alloy of lead containing 2 to 5% antimony is more easily cut than pure lead. The pantograph minification is related to the source-film and source-block distance. In another method, a roentgen-ray simulator with a tray at the proper distance permits the sketching of the block outline at the tray to cast a light shadow over the lungs in the roentgenogram.[25] In both of the above methods, the height of the blocks must be taken into account. A third method utilizes lead shot, No. 7½, to fill a styrofoam cavity 7.5 cm. deep. This thickness is equivalent to more than 5 cm. of solid lead. The cavity is cut in the styrofoam at the tray distance with a hot electrical wire supported at the target distance, as the other end of the taut wire is made to trace the lung outline on the roentgenogram at the film distance.[7] In the latter method, the edges of the blocking are parallel to the rays, but since the styrofoam holding the shot is opaque to light, the outline of the lung blocks is not seen upon the skin. A method which utilizes lead shot, but permits visualization of the light field upon the patient, has been described.[19,20] The shot is glued together in a thermoplastic material using polyethylene foam as a form cut with divergent sides in a manner similar to that described above. Alternatively, a low melting point alloy molded into a solid block may be used.[6]

DOSE UNIFORMITY BETWEEN ADJACENT FIELDS

It is possible to achieve uniformity of dose at the junction of 2 fields from geometric considerations, providing the light beam defines the dose which is 50% of the central axis dose of the penetrating beam. On most therapy machines, the edges of the light field define the position of 50% of the exposure in air or absorbed dose in free space at the central axis. At depth, the extension of the light edge approximates 50% of the dose on the central axis; the method described here is based on that assumption. The separation of the light fields at the skin is that necessary to achieve junction of the light fields at the chosen depth. This situation is illustrated in Figure 4 and is related to the length of the fields, L_1 and L_2, the SSD, and the depth beneath the surface where uniformity is to be achieved. By similar triangles, the separation S on the surface is calculated as shown. In practice, it is more difficult to achieve matching if the radiation field edge has a small penumbra; therefore, it is advisable not to use trimmers on the edges that are being matched.

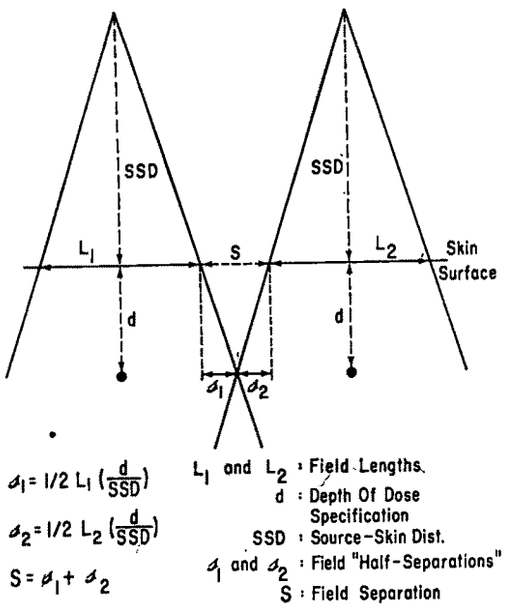


FIG. 4. Diagram illustrating the required field separation at the surface to achieve dose uniformity at depth between adjacent fields.

Similarly, it is advisable to shift the region of matching on different days of treatment, so that if errors are occurring, they will be spread over a distance. A more precise method based on decrement lines and experimental results has been given.[8,10]

If the fields are being treated over different periods of time, it may be advisable to treat the junction to a somewhat higher radiation dose in order to compensate radiobiologically for the longer total time of treatment. Johnson[17] treats the junction area to a dose 1.2 times greater than at the central axis when the courses of treatment to the adjacent fields occur at different times. This type of calculation is more complex than the one described above.[10]

DOSE TO SPINAL CORD

With parallel opposing fields, all parts between the surfaces are raised to nearly the same dose. If some sections are thinner, such as near the neck, then this region will receive a higher radiation dose than thicker body sections. The spinal cord may be protected by partial shielding of the upper portion down to about T_2, or by shielding of the entire spinal cord from the posterior for half the treatment;[25] however, from the latter, the reduction of tumor dose to the mediastinum might be an undesirable consequence. In Figure 5, the dose with 2 MV roentgen rays to the spinal cord in an Alderson phantom is compared to that delivered to the mediastinum with anterior and posterior mantle fields. The effect of shielding the upper part of the spine is also shown.

There will be differences in the dose to the spinal cord if the tumor dose is stated at or near the suprasternal notch or if it is stated lower in the mediastinum. Generally, the patient is thicker at the lower mediastinum and will therefore require a greater exposure to the anteroposterior and posteroanterior fields, with a resulting higher dose to the spinal cord. From a review of measurements at 12 institutions with lithium fluoride thermoluminescent dosimeters in an Alderson anatomic phantom, the average ratio of the maximum dose to the spinal cord to the prescribed dose in the mediastinum is 1.14 (range 0.93 to 1.36).[11] The beams included 2 MV roentgen rays, cobalt 60 gamma rays, 6 MV roentgen rays, 22 MV roentgen rays, and 33 MV roentgen rays. Although there have been few reports of neurologic symptoms in patients, some institutions may be very close to administering the maximum dose that can safely be delivered to the spinal cord.

Perhaps the best way of reducing the possibility of overdose to the spinal cord is by the use of compensating filters to attenuate those parts of the beam which will be treating thinner parts of the anatomy, such as the neck. The method proposed by Faw *et al.*[9] compensates in the craniocaudad and lateral dimensions of the patient, thus equalizing the doses in the axillary region as well as in the spinal cord. Another simpler method, which compensates only in the craniocaudad dimension and thus reduces the dose to the spinal cord, has been reported.[28] In this latter method, the tissue compensator is employed together with a beam-flattening filter for cobalt 60.

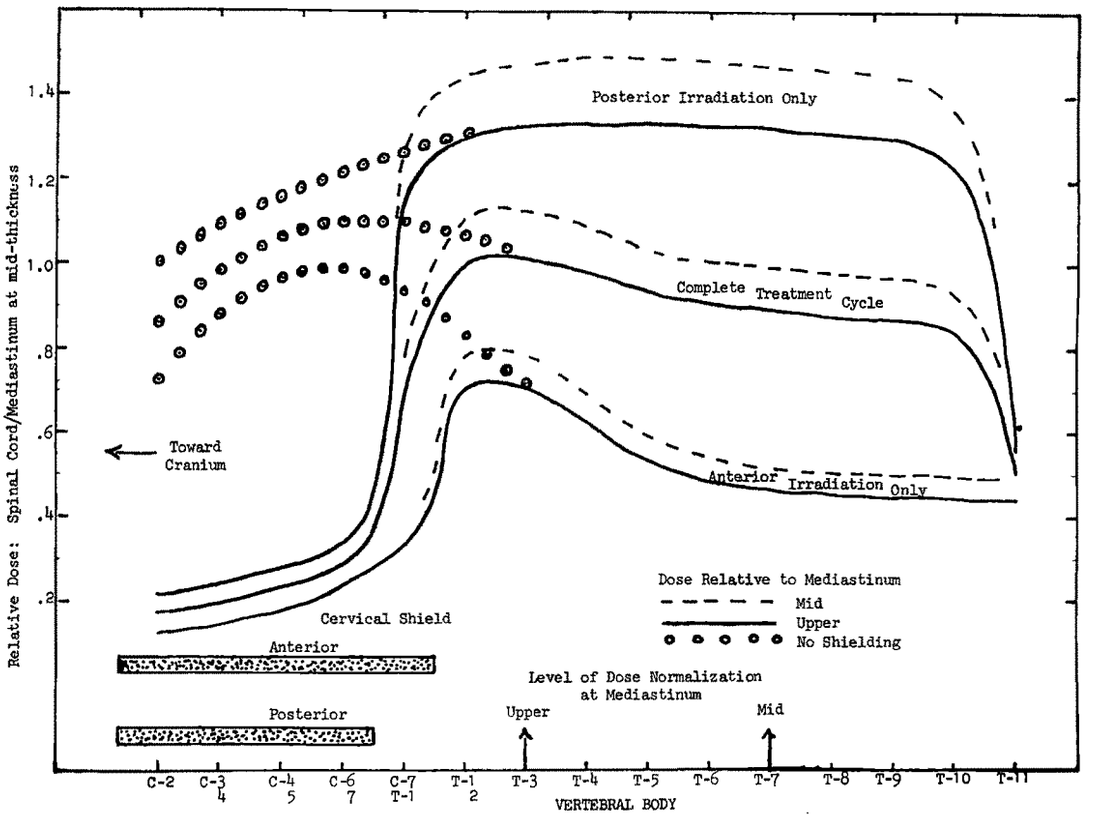


FIG. 5. The dose to the spinal cord from equally weighted anterior and posterior mantle treatment fields. The dotted lines are normalized to 1.00 at the mid-thickness of the mid-mediastinum (such as point C in Fig. 1); the solid lines are normalized to 1.00 at the mid-thickness of the upper mediastinum (such as point B in Fig. 1). The circles are a continuation of the solid lines, measured with no cervical shielding in place. Measurements were with 2 MV roentgen rays in an Alderson phantom at 150 cm. SSD.

DOSE TO GONADS OR FETUS

The dose to the gonads or to a fetus will depend on the particular field arrangement and distances. It is possible, however, to make some general statements about the doses. Usually it is possible to shield by blocking toward a cobalt 60 irradiator to reduce the radiation dose to the fetus or female gonads to approximately 20 rads from an upper mantle treatment delivering 4,000 rads to the mediastinum. Similarly, the male gonads can be protected to a large extent by exclusion from the radiation field.

Without additional blocking, however, Meurk and co-authors[21] indicate that approximately 65 rads are delivered to the ovaries from the mantle treatment with a mediastinal dose of 4,000 rads. Covington and Baker[4] investigated the dose at various distances from 6 MV roentgen rays and cobalt 60 gamma rays. A summary of their results is shown in Table VII.

SUMMARY

A general method is given for the cal-

TABLE VII

DOSE AT VARIOUS DISTANCES OUTSIDE THE EDGE OF A MANTLE FIELD AS A PER CENT OF THE DOSE AT MID-DEPTH IN THE CENTER OF THE FIELD

Distance from Edge of Field	6 MV Roentgen Rays	Co^{60}
5 cm.	3.7%	4.4%
10 cm.	1.6%	2.2%
15 cm.	0.8%	1.4%
20 cm.	0.5%	1.0%
25 cm.	0.3%	0.7%

From Covington and Baker, 1969.

culation of absorbed dose to an arbitrary point in an irregularly shaped radiation field. This method is recommended either as a routine method or as a standard method against which more rapid approximate methods may be judged for correctness.

In addition, limited consideration is given to the problems of secondary blocking, matching adjacent fields, dose to spinal cord, and dose to the gonads or fetus.

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STAGE I AND II NON-HODGKIN'S LYMPHOMA*

RESULTS OF REGIONAL RADIATION THERAPY

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THE futility which underlies the seemingly casual approach to the treatment of Hodgkin's disease has been dispelled in all but the naive. When appropriately evaluated and treated, 8 out of every 10 patients with Hodgkin's disease should be cured.[6] If only Stage I and II Hodgkin's disease is considered, recent results reported show nearly all patients being controlled when appropriately treated with irradiation.[6] In the case of an early stage non-Hodgkin's lymphoma, diagnostic and therapeutic futility exists not only in its naive form, but occasionally efforts approach disparaging dimensions.

There is some foundation in the literature of the 1940s and 1950s for this seemingly fatalistic attitude toward the treatment of these disease entities. Craver in 1947 reported some 300 patients with malignant lymphomas and could claim only a 25 per cent 5 year survival.[2] Similar figures as seen in Table I are found throughout the literature of that era. Even as late as 1960, Cook *et al.*[1] could only report a 29 per cent 5 year survival for all lymphomas. It was during this same period that Vera Peters was achieving greater than a 50 per cent 5 year survival in Stage I disease.[10] Scheer also was reporting a 50 per cent 5 year survival in Stage I reticulum cell sarcomas and 75 per cent surviving free of disease in Stage I lymphosarcomas.[11]

This rather striking improvement in the reported results was brought to the forefront in 1971 by the report of Lipton and Lee[8] with the truly gratifying results of 85 per cent 4 years free of disease in Stage I lymphosarcoma and reticulum cell sarcoma. These successes have been overshadowed by the marked improvement and satisfaction obtained with the treatment of Hodgkin's disease. Such fine results as are now being achieved warrant an approach which is thorough and comprehen sive.

Improved results at the present time may be due to one or a combination of factors. There has been an introduction of supervoltage radiation which allows the delivery of an adequate dose to an appropriate volume of tissue. In the interim, modern diagnostic techniques such as lymphography, vena cavagraphy, intravenous pyelography, and laparotomy have become nearly routine procedures. These studies have allowed better definition of disease below the diaphragm and in the

TABLE I

REVIEW OF CASES COLLECTED FROM THE LITERATURE

Author	Year	5 Year Survival	
		No. of Patients	Per Cent
Hamann[3]	1948	43	12
Stout[13]	1947	119	23
Craver[2]	1947	308	26
Hare *et al.*[4]	1948	181	29
Lenz *et al.*[7]	1950	242	27
Nichols *et al.*[9]	1957	71	26
Hilton and Sutton[5]	1962	65	29
Cook *et al.*[1]	1960	211	29
Peters[10]	1963	102	51
Scheer[11]	1963	77	75
Lipton and Lee[8]	1971	26	85 (4 yr.)

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TABLE II
NUMBER OF PATIENTS
(1960–1970)

Lymphosarcoma	33
Reticulum cell sarcoma	20
Giant follicular lymphoma	12
Total	65

viscera. The addition of bone marrow biopsy, complete chest roentgenography, skeletal survey, liver and spleen scans, all contribute to minimizing errors in staging the lymphomas. Certainly the refinement in pathologic evaluation of the tissue submitted has provided even greater clarification of the problem in the non-Hodgkin's lymphoma. All of these factors may influence survival figures. Certainly better results are being achieved.

MATERIAL AND METHOD

The material compiled in the present study consists of 65 patients who had biopsy proved non-Hodgkin's lymphomas (Table II). The population studied all had Stage I and II non-Hodgkin's lymphomas and was referred to the Radiotherapy Service at either Rush-Presbyterian-St. Luke's Medical Center or the Lutheran General Hospital during the period of 1960 to 1970. Table III outlines the staging system utilized following evaluation of these patients.

None of the patients included here have been previously treated with any form of therapy. Staging was based upon clinical examination and available roentgenographic studies. In addition, other tests when utilized were included for staging purposes. It should be emphasized that not all patients had lymphangiography or bone marrow aspiration in their routine evaluation.

TABLE III
STAGING SYSTEM UTILIZED

Stage I —Disease limited to 1 anatomic region or 2 contiguous regions on the same side of the diaphragm
Stage II—Disease in more than 2 anatomic regions or 2 noncontiguous regions on the same side of the diaphragm

All patients included in the study were treated by supervoltage radiation utilizing cobalt 60 teletherapy. A minimum dose of 3,000 rads in 3 weeks for a nominal single dose equivalent of 1,100 rets up to 4,000 rads in 4 weeks for a nominal single dose equivalent of 1,320 rets was given. Therapy was administered to a generous treatment volume including the area of involvement and the adjacent lymph node groups.

Patients who developed persistent disease in the treatment volume or in a distant site were considered treatment failures. In addition, patients who were lost to follow-up were considered as failures in this review.

In the current series approximately 25 per cent of the cases show their initial involvement in an extra-nodal site while approximately 75 per cent of the cases were confined to the lymph node groups.

EVALUATION OF RESULTS

We will attempt to evaluate the data in the current study from several viewpoints. Here we consider the classical disease entities of lymphosarcoma, reticulum cell sarcoma, and giant follicular lymphoma. The reasons for this nomenclature are several. First, it is the diagnosis that was attached to the patient at the time he was treated. Secondly, this nomenclature is still being used in the majority of institutions today. Thirdly, it would allow better comparison with what has been previously recorded.

After considering each of the disease categories, we will show the combined results of all forms of early stage non-Hodgkin's lymphoma.

In Tables IV and V can be found the re-

TABLE IV
SIX YEAR SURVIVAL STAGE I AND II
LYMPHOSARCOMA

No. of Patients	Per Cent Surviving Free of Disease
33	92

TABLE V

LYMPHOSARCOMA

Months at Risk	No. of Patients	Failures	Patients Free of Disease	Per Cent Surviving Free of Disease
12 or more	33	3	30	91
24 or more	33	5	28	85
36 or more	25	3	22	88
48 or more	19	2	17	89
60 or more	15	2	13	87
72 or more	12	1	11	92

sults we have achieved in lymphosarcoma. Thirty-three patients were seen during the 1960 to 1970 interval. The over-all results in the group are 92 per cent patients surviving free of disease at 6 years. One may see particularly in Table v a breakdown, on a year by year basis, showing that this percentage remained relatively constant after 12 to 18 months following treatment.

In Tables VI and VII is an analysis of the

TABLE VI

SIX YEAR SURVIVAL STAGE I AND II RETICULUM CELL SARCOMAS

No. of Patients	Per Cent Surviving Free of Disease
20	70

results achieved in the Stage I and II reticulum cell sarcomas. In these 2 tables one can see that there were 20 patients in the review and that of those at risk 6 or more years, 70 per cent were alive and free of disease.

In Table VII one can appreciate that small numbers of patients do not lend themselves to statistical analysis. A shift of 1 patient in the group at risk 24 months or less would have made the survival statistics in this group almost exactly the same as in the groups 3 or more years at risk. Similarly, a shift of 1 patient from success to failure in the 6 year group would have made the survival figures similar to those obtained in patients at risk for a shorter period of time.

Tables VIII and IX depict the result of radiation therapy in the early stage of giant follicular lymphomas. Here even fewer patients are available for analysis. There was a total of 12 patients and the survival figures free of disease are 75 per cent of those at risk 6 years or more, and are similar to those at risk 1 year or less.

Finally, we combined all of the patients into 1 group and called them Stage I and II non-Hodgkin's lymphomas and then calculated the 6 year survival free of disease rate. As we have said before, the total group consisted of 65 patients and of those

TABLE VII

RETICULUM CELL SARCOMAS

Months at Risk	No. of Patients	Failures	Patients Free of Disease	Per Cent Surviving Free of Disease
12 or more	20	8	12	60
24 or more	20	8	12	60
36 or more	14	4	10	71
48 or more	13	4	9	69
60 or more	13	4	9	69
72 or more	10	3	7	70

TABLE VIII

SIX YEAR SURVIVAL STAGE I AND II GIANT FOLLICULAR LYMPHOMA

No. of Patients	Per Cent Surviving Free of Disease
12	75

TABLE X

SIX YEAR SURVIVAL FREE OF DISEASE STAGE I AND II NON-HODGKIN'S LYMPHOMAS

No. of Patients	Per Cent Surviving Free of Disease
65	81

at risk 6 or more years the 5 year survival free of disease period was 81 per cent (Table x). To be succinct, 26 patients were treated 6 or more years ago and 21 of the 26 were surviving free of disease at 6 years.

CONCLUSION

Today, no approach to therapy is complete without adequate definition of the disease. It would seem that the literature supports thorough pretherapeutic evaluation of non-Hodgkin's lymphomas so that appropriate staging can be accomplished and therefore appropriate therapy given. Our own results approach those recorded in the recent literature.

The importance of pathologic diagnosis is paramount in developing an evaluation and therapeutic regimen. Once the correct pathologic diagnosis is established in non-Hodgkin's lymphoma, the evaluation should be rather uniform with exceptions being made for the general status of the patient. Certainly serious consideration should be given to lymphangiography, liver and spleen scanning, intravenous pyelography, appropriate chest roentgenography, and, when available, a so-called total body scintillation scanning.

There is still controversy over the benefit of surgical staging in patients with non-Hodgkin's lymphomas. The results reported from various centers already utilizing this technique indicate that there may well be an advantage to considering this as a diagnostic adjunct in these disease entities as well as in Hodgkin's disease.[13,14] It would certainly seem wise to employ the technique if the staging procedure, staging laparotomy, would determine whether definitive curative therapy could be undertaken or whether the patient should be relegated to palliative or protocol therapy.

There is a tendency at the present time to advocate that the treatment of non-Hodgkin's lymphoma be similar to the treatment of Hodgkin's disease. The literature does not necessarily support this concept. In the reports of Seydel *et al.*[12] it is suggested that a dose lower than 4,000 rads may be adequate; in fact, for giant follicular lymphoma, a dose as low as 2,000 rads in 2 weeks may be sufficient to permanently control the disease. The work of Vera Peters[10] also suggests that radically extended treatment fields in non-Hodgkin's lymphomas may not be indicated. From our own work and a review of the literature

TABLE IX

GIANT FOLLICULAR LYMPHOMA

Months at Risk	No. of Patients	Failures	Patients Free of Disease	Per Cent Surviving Free of Disease
12 or more	12	3	9	75
24 or more	10	2	8	80
36 or more	8	2	6	75
48 or more	7	2	5	72
60 or more	4	1	3	75
72 or more	4	1	3	75

it would seem that, if the patient has had adequate pretherapeutic evaluation and if he is found to have a Stage I or II non-Hodgkin's lymphoma, the following course of treatment is indicated: a tumor dose of 3,000 rads in 3 weeks should be delivered to a treatment volume including the involved and adjacent echelons of lymph nodes; an additional 500 rads should be given to the involved area.

Optimal treatment of this disease has not been defined and probably will not be defined until adequate cooperation is developed, so that a large population of patients can be appropriately studied.

SUMMARY

A review of the literature and our own work suggests that the clinical Stage I and II non-Hodgkin's lymphoma deserves thorough pretherapeutic evaluation and aggressive regional treatment, and that, when this is done, a favorable prognosis can be expected.

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RADIATION THERAPY OF GENERALIZED LYMPHOCYTIC LYMPHOMAS*

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RADIATION therapy has been relegated to an increasingly minor role for the primary management of patients with malignant lymphomas of the well-differentiated and poorly-differentiated types (lymphosarcoma or LSA). Widespread involvement is clinically present in most cases at the time of diagnosis, thereby dissuading radiotherapists from attempting definitive treatment, and irradiation has usually been confined to the palliation of local symptoms. Limited radiotherapy techniques used alone fail to effectively control the over-all disease process and do not consistently yield symptom-free intervals of significant duration. Furthermore, the survival rates for the radiotherapeutic management of LSA are substantially inferior to those now being achieved in Hodgkin's disease.[6] The need for systemic treatment is apparent and there has been a paucity of articles directed toward the radiation therapy of generalized LSA during the past decade.[1,3] It has been correctly stated[2] that "radiotherapy has been replaced to a large extent by chemotherapy in the treatment of generalized lymphosarcomatous disease."

As an alternative approach to chemotherapy, we undertook the investigation of more extensive radiotherapy techniques in 1964 in order to study the potential for achieving relatively complete if not complete control of disease in cases with anatomically generalized involvement. Our early experience[4] suggested that at least certain clinical presentations appeared amenable to primary management with irradiation. Patients with widespread lymph node involvement occasionally had complete clinical remissions after radiotherapy, even when bone marrow invasion by lymphoma had been documented prior to treatment. Remissions were prolonged in some cases without the addition of maintenance therapy following initial remission induction;[5] and with further case accession into this program, it is now possible to more definitively evaluate the results of radiation therapy from the standpoint of initial response rates, the duration of the first remissions, and the preliminary survival rates.

METHODS

Since 1965, a total of 29 consecutive patients with previously untreated lymphocytic lymphoma have been admitted and treated with primary radiotherapy. These cases were histologically subclassified by Dr. Gregory T. O'Conor, Head of Surgical Pathology at the National Cancer Institute, on the basis of the predominant tumor cell type and the growth pattern. The diagnosis was well-differentiated lymphocytic, diffuse type in 2 cases, well-differentiated nodular in 5 cases, poorly-differentiated diffuse in 6 cases, and poorly-differentiated nodular in the remaining 16 cases. The median age at diagnosis was 44 years (range 24 to 64) and 20 of the 29 patients were male.

On a clinical basis alone, nearly all patients were readily determined to have anatomically extensive disease. Diffuse lymphadenopathy was palpable above and below the diaphragm in 25 of the 29 cases. Thus, although bipedal lymphography and other usual staging studies were routinely performed, rigorous diagnostic evaluation was generally not required to determine the presence of extensive disease. No patient had a lymphocytosis in the peripheral blood,

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although 7 patients had bone marrow invasion with lymphoma identifiable on biopsy. Those patients with evident disease in extranodal sites other than the bone marrow are excluded from this review.

Eighteen patients were treated with total body irradiation (TBI) using a technique[5] which consisted of 10 rads (midline absorbed dose) administered at the rate of 3–5 times per week to a total dose of 100–300 rads. In some instances, TBI was interrupted midway to permit hematologic recovery. For some patients, a total dose of 100–150 rads of TBI was followed by the systematic irradiation of all major lymph node areas above and below the diaphragm (total nodal irradiation or TNI). When TNI was preceded by TBI in this manner, a 2 or 3 month interval was interposed to permit bone marrow recovery before commencing with TNI.

Eleven patients were treated only with TNI, using a modification of the treatment plan for Hodgkin's disease as to include the routine irradiation of Waldeyer's ring, preauricular areas, the epitrochlear and the very low femoral regions. When massive retroperitoneal or mesenteric involvement was present, "abdominal bath" irradiation of the entire peritoneal cavity was employed. The various anatomic segments irradiated during TNI were sequentially treated with daily tumor doses of 150–200 rads to a dose of 2,000–3,000 rads. Treatment was given on an ambulatory outpatient basis except when poor general condition related to advanced disease dictated the necessity for hospitalization.

Following completion of initial treatment, patients having remission of disease were observed without further therapy until relapse of disease was documented. When relapse was established, treatment was reinstituted even though many patients remained clinically asymptomatic. Either local irradiation or TBI was selected for secondary treatment, depending upon the apparent extent of disease at the time of relapse. Chemotherapy was consistently withheld until it was decided that additional radiotherapy would no longer offer major benefit or potential control of the systemic disease process. Thus to date, only 5 of the 29 patients have received chemotherapy, 3 of whom have expired. The overall survival rates have not been materially influenced by treatment other than irradiation, as only 2 of the 5 patients treated with chemotherapy received improvement from chemotherapy.

RESULTS

In defining the response to therapy, complete remission implies total disappearance of clinical, radiographic, and laboratory (including bone marrow) evidence of disease together with resolution of related symptoms for a minimum of 2 months. The complete remission rate achieved with initial therapy in this series was 93 per cent (27 of 29 patients). Patients were then observed without further therapy and the median duration of unmaintained remission was 26 months (range 3–60). No patient has died from intercurrent disease and the uncorrected survival rate calculated actuarially is shown in Figure 1. The 3 year and 5 year survival rates are 86 per cent and 72 per cent, respectively.

Treatment was generally administered on an outpatient basis and was well tolerated. The usual local reactions were observed during TNI such as anorexia, pharyngitis, esophagitis, and occasional diarrhea. The lower tumor doses than used for Hodgkin's disease minimized the hematologic toxicity, and serious normal tissue reactions such as pneumonitis and pericarditis have not been observed. Four of the 18 patients treated either with TBI alone or in combination with TNI required transient blood transfusions for serious hematopoietic depression. Hematologic complications did not occur, however, and systemic infections were not observed during periods of radiation-induced leukopenia. There was consistent return of peripheral blood cell counts to normal in those patients having a clinical remission of at least 6 months' duration. The non-remitters and

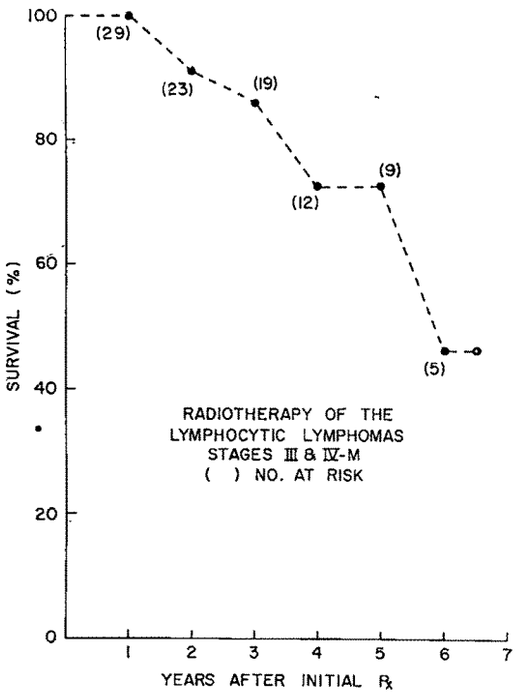


FIG. 1. The survival rates are actuarially calculated for 29 consecutive patients with previously untreated lymphocytic lymphoma. Stages III and IV–M refer to the absence and presence of bone marrow invasion respectively in patients with generalized lymph node involvement. Treatment consisted of "systemic radiotherapy" using total body irradiation or other wide-field techniques.

those with very brief remissions obviously had further compensation of hematopoietic function secondary to additional treatment and/or progression of their disease.

DISCUSSION

This experience forcefully illustrates the philosophical difference between employing radiation therapy for palliation of local symptoms *versus* its use as a modality of systemic therapy. While symptom-directed irradiation may be temporarily beneficial for generalized lymphoma, the "chasing" approach fails to effectively control the over-all disease process, seldom provides prolonged intervals of disease-free survival, and eventually results in a decompensation of bone marrow function and intolerance to further therapy. Thus, the absence of systemic treatment results in a clinical course typified by the development of new symptoms with distressing rapidity and a continuing attempt to maintain patients in a reasonable functional status.

In contrast, more comprehensive treatment, as described here, has produced complete remissions of substantial durability and thereby afforded patients relatively long intervals of normal function. The preliminary median survival rate in excess of 5 years also indicates that high remission rates associated with prolonged remissions are reflected in correspondingly increased survival, a sequence of events dramatically emphasized by progress in the acute leukemias. So it is the opinion of this author that radiotherapy no longer deserves to be replaced "to a large extent by chemotherapy in the treatment of generalized lymphosarcomatous disease." However, caution *is* deserved when radiation therapy is adopted as the primary form of treatment; radiotherapists should become conversant with the use of irradiation as a systemic modality and abandon their conventional techniques of high dose treatment limited to clinically involved or symptomatic areas of disease.

SUMMARY

The overwhelming majority of patients with malignant lymphomas of the lymphocytic type present with generalized disease at the time of diagnosis. The consequent need for systemic therapy has resulted in the adoption of chemotherapy as the accepted form of treatment.

As an alternative, we have investigated "systemic radiotherapy" utilizing total body irradiation and other wide-field techniques.

The experience described in this report concerns a consecutive series of patients with generalized lymph node involvement on admission. Cases with documented lymphomatous invasion of the bone marrow are included, while those with involvement of other extranodal sites have been excluded from this review.

The complete remission rate was 93 per cent (27 of 29 patients) and the median duration of remission *without* maintenance therapy was 26 months.

Following relapse, irradiation was again employed effectively in most instances.

Response to therapy was not related to the histologic degree of tumor cell differentiation and was not affected by the presence of bone marrow involvement.

A 3 year survival rate of 86 per cent demonstrates the potentially important role for radiation therapy despite the existence of anatomically widespread involvement.

It must be recognized, however, that the radiotherapy approach should be comprehensive and aimed at control of the entire systemic process rather than limited to the palliation of symptomatic regions.

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LYMPHOSARCOMA

TREATMENT AND END RESULTS IN 355 PATIENTS*

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THE modalities of treatment and end results of 355 patients with lymphosarcoma, treated at the Pack Medical Group, are presented in this report. A previous report dealt with the treatment and end results in 567 patients with lymphosarcoma, from 1945 to 1957.[1] All patients in these 2 groups were private patients of the Pack Medical Group, and the therapeutic principles—surgical, radiologic and chemotherapeutic—were applied through the collective experience and judgment of a few members of this Group. The statistical significance of this report may be related to the unified principles of therapy used in these patients.

MATERIAL

In the present series of 355 patients, there were 260 patients with lymphosarcoma, 71 with reticulum cell sarcoma, and 24 with giant follicular lymphosarcoma.

CLINICAL STAGING OF PATIENTS WITH LYMPHOSARCOMA

The clinical staging adopted for Hodgkin's disease was employed in this series of patients.[3]

A detailed work-up was done on each patient, including a complete history and physical examination. A careful review of any submitted biopsy specimens of lymph nodes was made by Doctor George K. Higgins, Consultant Pathologist of the Pack Medical Group.

Radiologic studies of the chest and, if indicated, tomograms of the mediastinum and lungs, were obtained. Bilateral lymphangiography was selectively done on most patients, unless specifically contraindicated. Intravenous pyelography, liver and spleen scannings, and in selected instances inferior vena cavagraphy, were carried out. In addition, a skeletal survey, upper gastrointestinal series (a small bowel series, if indicated), and a barium enema examination, preceded by a sigmoidoscopy, were routinely done.

A complete biochemical profile was obtained in all patients, as well as a complete hemogram, including a differential white blood cell count. A serum electrophoretic pattern was obtained, and an immune globulin fractionation was selectively done. Studies for hemolysis were carried out on all patients.

In instances of equivocal lymphangiography, exploratory laparotomy, including a splenectomy and liver biopsy, were selectively performed. In women of child-bearing age, the ovaries were laterally moved out of the intended ports of irradiation and marked with sterile clips.

In addition, patients with primary extranodal lymphosarcoma were evaluated as a group. In the present series, of the 355 patients, there were 31 patients with Stage I disease, 120 patients with Stage II disease, 159 patients with Stage III disease, 24 patients with Stage IV disease, and 21 patients with primary extranodal disease.

APPROACHES TO TREATMENT

The various approaches to treatment include:

1. Radiation therapy
   a. Definitive in Stage I
   b. Possibly definitive in Stage II
   c. Palliative in Stages III and IV
2. Surgical treatment
   a. Definitive in selected patients with unicentric lymphosarcoma

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From the Pack Medical Foundation, New York, New York.

b. Palliative, *e.g.*, to relieve intestinal obstruction or remove bulky masses of tumor
3. Chemotherapy
   a. Alkylating agents
   b. Vinca alkaloids
   c. Hormones
   d. Antimetabolites
   e. Antibiotics
   f. Combined chemotherapy
4. Radioactive isotopes
5. Combinations of the above

SURGERY AND IRRADIATION IN STAGE I LYMPHOSARCOMA

Treatment may include either surgery or irradiation or a combination of both in a proven unicentric or unifocal patient with lymphosarcoma.

Surgery may be the preferred initial treatment in a small select number of patients. Surgery may be indicated when unicentric lymphosarcoma is found: (1) in the upper third of the neck; (2) in the lower part of the axilla; (3) in the femoral fossa; (4) as a primary focus in any portion of the gastrointestinal tract; and (5) as a primary focus in a single organ.

It is imperative that any additional foci of lymphosarcoma be excluded before a radical surgical approach is entertained as a form of treatment. Lymphangiography is indispensable in selecting patients for radical axillary or groin dissection.

Postoperative Irradiation. Once healing has occurred, 3,500 to 4,000 rads is delivered to the tumor bed over a period of 4 to 5 weeks, using the cobalt 60 teletherapy unit or the supervoltage generator. A higher dose is used in the instances of reticulum cell sarcoma.

There were 5 patients in the present series who were treated with a combination of radical surgery and elective postoperative irradiation.

RADIATION THERAPY OF LYMPHOSARCOMA STAGES I AND II

Most patients with lymphosarcoma are not eligible for surgery, and irradiation is the preferred method of treatment in these cases.

In patients with Stage I and Stage II lymphosarcoma, a "curative" radiotherapeutic approach is used, delivering 3,500 to 4,500 rads over a period of 4 to 5 weeks. Patients with reticulum cell sarcoma were given the higher dose.

Either cobalt 60 teletherapy or supervoltage therapy was used to treat the current series of patients initially. One of 2 treatment plans was employed.

In the first, "extended field" cobalt 60 teletherapy was used, irradiating the involved area and contiguous lymph node-bearing regions. If the disease appeared to be localized, 3,500 rads were delivered over a period of 3 weeks in patients with lymphosarcoma. The contiguous lymph node-bearing regions were given 3,000 rads.

In patients with reticulum cell sarcoma, a dose of 4,500 rads was given over a period of 4 to 5 weeks. If the disease was resistant, we have given as much as 5,000 rads to the involved region. The contiguous lymph node-bearing regions were given at least 3,000 rads. A previous study by the author indicated a lower recurrence rate of the disease activity when the contiguous lymph node regions were adequately irradiated.[2]

In the second, supervoltage therapy was used, employing a linear accelerator to deliver to an upper mantle port 3,500 to 4,500 rads in a 4 to 5 week period of time. The higher dose is used in reticulum cell sarcoma. Where possible, after delivering 3,000 rads, the width of the mediastinal port is reduced to avoid excessive irradiation of the lung parenchyma.

Where disease was localized below the diaphragm, an inverted "Y" port, covering the inguinal, iliac and paraaortic regions, was employed, delivering 3,500 to 4,500 rads over a 4 to 5 week period, the higher dosage being given to those patients with the histologic picture of reticulum cell sarcoma. The spleen, considered to be a part of the lymphatic system, has routinely been included in the field. When a splenec-

tomy has been performed, 2,500 rads has been delivered to the splenic bed, outlined by opaque clips at the time of surgery. The width of the paraaortic field is reduced after 3,000 rads, when possible, to avoid excessive irradiation of the adjacent tissues.

STAGE III

In patients with Stage III lymphosarcoma, in good clinical condition, an upper mantle port has been employed, as well as an inverted "Y" port, delivering a possible 2,500 to 3,500 rads to each region over 3 to 4 weeks. An interval of 3 to 4 weeks of rest is allowed between courses of treatment.

STAGE IV

In patients in good condition clinically, who present with involvement of nodal and extranodal structures, such as the skin, skeleton, gastrointestinal tract, liver or spleen or other single organs, palliative irradiation to the involved structures and lymph node regions is given. When possible, 1,800 to 3,000 rads is administered to the involved region and, where feasible, either an upper mantle or inverted "Y" port, or both, is used, delivering in general lower dosages, such as 1,200 to 2,500 rads over a 2 to 3 week period of time.

THERAPY OF PRIMARY EXTRANODAL DISEASE

In instances of single organ involvement, surgical extirpation, along with regional lymph node dissection has been carried out. Following wound healing, 3,500 to 4,500 rads has been delivered to the tumor bed over a 3 to 4 week period of time.

CHEMOTHERAPY

Chemotherapy has been employed to control the constitutional symptoms in patients with Stage IIB, Stage IIIB, and Stage IV lymphosarcoma, at times prior to radiation therapy. When constitutional symptoms are present in patients with Stage IIIB and Stage IV lymphosarcoma, chemotherapy has generally been employed prior to instituting radiation therapy. A suitable interval of time following chemotherapy is necessary before irradiation is given, to allow the bone marrow to recover.

END RESULTS

Of 355 patients in the present series, 74 per cent survived 3 years and 60.2 per cent survived 5 years or longer as illustrated in Figure 1.

STAGE I

Thirty-one patients with Stage I lymphosarcoma experienced a 100 per cent 3 year and 84 per cent 5 year survival. There were 5 patients in this group with a unicentric focus of disease who underwent an initial radical surgical procedure. All of these patients lived 5 years, and it is hoped that they may represent a potential cure.

Of the remaining 26 patients with Stage I

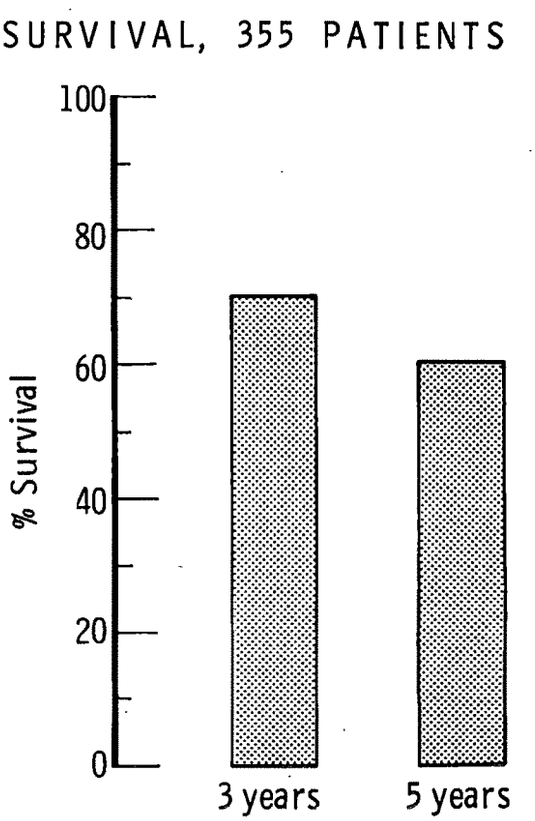


FIG. 1. Lymphosarcoma. Of 355 patients, 74.1 per cent lived 3 years and 60.2 per cent lived 5 years.

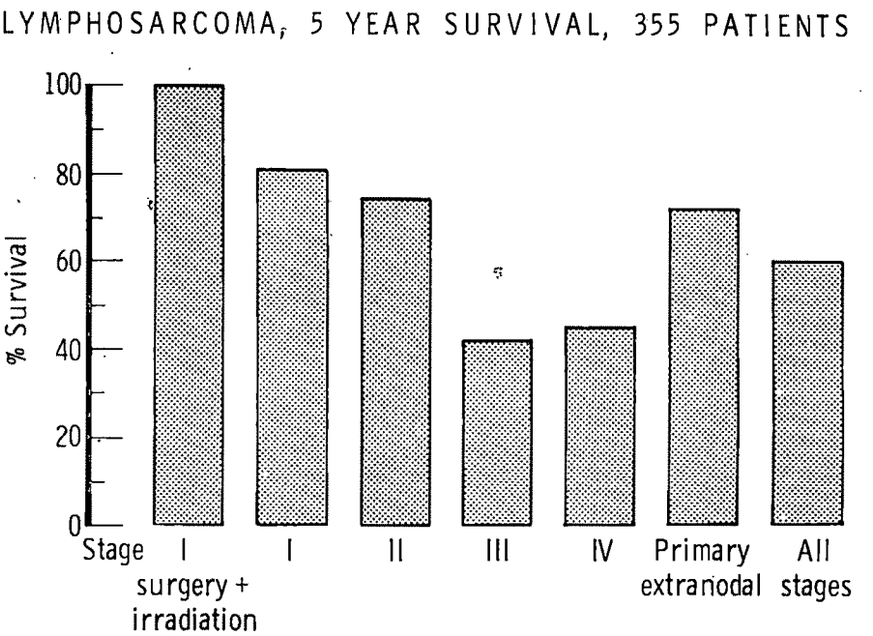


FIG. 2. Five year survivals in the various stages of lymphosarcoma. A 100 per cent 5 year survival of patients with lymphosarcoma amenable to surgery and irradiation occurred; in other Stage I patients, there was an 81.0 per cent survival. In patients with Stage II disease, there was a 74.1 per cent 5 year survival; a 42.8 per cent 5 year survival occurred in patients with Stage III lymphosarcoma; and in patients with Stage IV disease, a 45.8 per cent 5 year survival was found.

Of patients with primary extranodal lymphosarcoma, 71.4 per cent lived 5 years.

disease, and treated with irradiation only, there was a 100 per cent survival rate for 3 years and an 81 per cent survival rate for 5 years.

STAGE II

There was a total group of 120 patients with Stage II lymphosarcoma. The 3 year survival rate was 84.2 per cent and the 5 year rate was 74.1 per cent.

Fifty-three patients with Stage IIA lymphosarcoma had an 88.6 per cent 3 year survival and a 79.2 per cent 5 year survival rate. Of 67 patients with Stage IIB lymphosarcoma, 80.6 per cent lived 3 years and 70.1 per cent lived 5 years.

STAGE III

Of 159 patients with Stage III lymphosarcoma, 52.8 per cent lived 3 years and 42.9 per cent lived 5 years.

There were 89 patients with Stage IIIA lymphosarcoma, with a 60.7 per cent 3 year survival and a 52.8 per cent 5 year survival rate.

Of 70 patients with Stage IIIB lymphosarcoma, 51.4 per cent lived 3 years and 42.9 per cent lived 5 years.

STAGE IV

Fourteen (58 per cent) of 24 patients with Stage IV lymphosarcoma lived 3 years and 9 patients (45.8 per cent) lived 5 years.

PRIMARY EXTRANODAL DISEASE

Of 21 patients, 85.7 per cent with primary extranodal disease lived 3 years and 71.4 per cent lived 5 years.

Figure 2 illustrates the survival in the different stages of lymphosarcoma.

HISTOLOGIC TYPE OF LYMPHOSARCOMA AND LONGEVITY

In general those patients classified as having giant follicular lymphosarcoma lived the longest, whereas those with reticu-

lum cell sarcoma had the shortest survival. The patients with giant follicular lymphosarcoma experienced an 83 per cent 5 year survival. Those with lymphosarcoma had a 61 per cent 5 year survival and 56 per cent of those with reticulum cell sarcoma lived 5 years.

SUMMARY

Appropriate study and proper staging of every patient with lymphosarcoma are mandatory in the management of this disease.

Radiation therapy is the principal and preferred form of treatment for most patients with lymphosarcoma.

Patients with unicentric lymphosarcoma should receive 4,000 to 4,500 rads of radiation to the involved site with 3,000 to 3,500 rads to adjacent lymph node-bearing regions.

In a few selected patients, surgical extirpation may be useful. A tumor dose of irradiation should be given these patients following wound healing. Patients with regional lymphosarcoma should be treated with at least 3,500 rads to the diseased sites and 3,000 rads to the adjacent lymph node-bearing regions.

Patients with generalized nodal lymphosarcoma should be given total nodal irradiation whenever feasible, employing, if possible, 3,000 to 3,500 rads. In those in poor clinical condition, when radiation therapy is not feasible, chemotherapy should be employed.

Patients with Stage IV lymphosarcoma, who cannot be given irradiation, should receive chemotherapy to control their disease as long as possible.

Patients with primary extranodal lymphosarcoma should have surgical excision of their tumor and dissection of the adjacent lymph node-bearing regions whenever possible. This should be followed by a full tumor dose of irradiation to the tumor bed.

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LYMPHOSARCOMA IN CHILDREN

A ROENTGENOLOGIC AND CLINICAL EVALUATION OF 60 CHILDREN

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LYMPHOMAS represent about 14 per cent of the malignant neoplasms found in the pediatric population.[3] Excluding Hodgkin's disease the incidence ranges from 3 to 10 per cent.[4,16]

Numerous reports cite the clinical course of a few unusual cases, some with interesting roentgenographic features.[8,12,21,26] Several large series emphasize primarily the clinical course, therapy and prognosis,[2,3,5,10,15,16,27] while others consider the roentgenographic features of lymphosarcoma only as it relates to particular organ systems.[1,6,7,11,13,17–20,22]

The roentgenographic features, noted in all reports referring to them, manifest themselves with varying rates of occurrence, from infrequent to very frequent.

It is the purpose of this report to document both the clinical and roentgenographic findings in 60 infants and children with lymphosarcoma.

MATERIAL AND METHOD

The records of 60 children with lymphosarcoma were reviewed and evaluated. The data included information relating to the patient's sex, age, site of initial involvement, cell type, clinical signs and symptoms, conversion to leukemia, and survival. The nature of therapy was also noted, but not analyzed in detail.

The roentgenograms of each patient were reviewed. The films available were obtained because of a specific presentation or manifestation of the individual's disease course. Survey examinations were not routinely obtained in the course of an evaluation of lymphosarcoma at The Children's Memorial Hospital. The frequency of involvement of any one organ system was derived from the specific films available. The roentgenographic findings of each patient were documented.

CLINICAL DATA

Sex. Of the 60 patients, 49 were male and 11 were female (approximate ratio of 4.5:1, M:F).

Age. The ages of the patients ranged between 1 year and 16 years (Chart 1). Patients older than 16 years are not admitted to The Children's Memorial Hospital, unless they were previously evaluated at the institution. The distribution of ages suggests a bimodal occurrence with peaks at 5 and 12 years. No patient younger than 1 year appears in the series.

Cell type. The most frequent cell type noted was either a small or a large lymphoblast (LB). The total "LB" group numbered 49 (41 males and 8 females). A more mature type cell was recognized on 6 occasions. These were considered lymphocytic lymphosarcomas ("LC"; 5 males and 1 female). There were 5 reticulum cell sarcoma patients ("R"; 3 males and 2 females).

Primary site of involvement. The primary site of involvement was indicated by the clinical signs, symptoms, or findings. The initial roentgenographic findings did not

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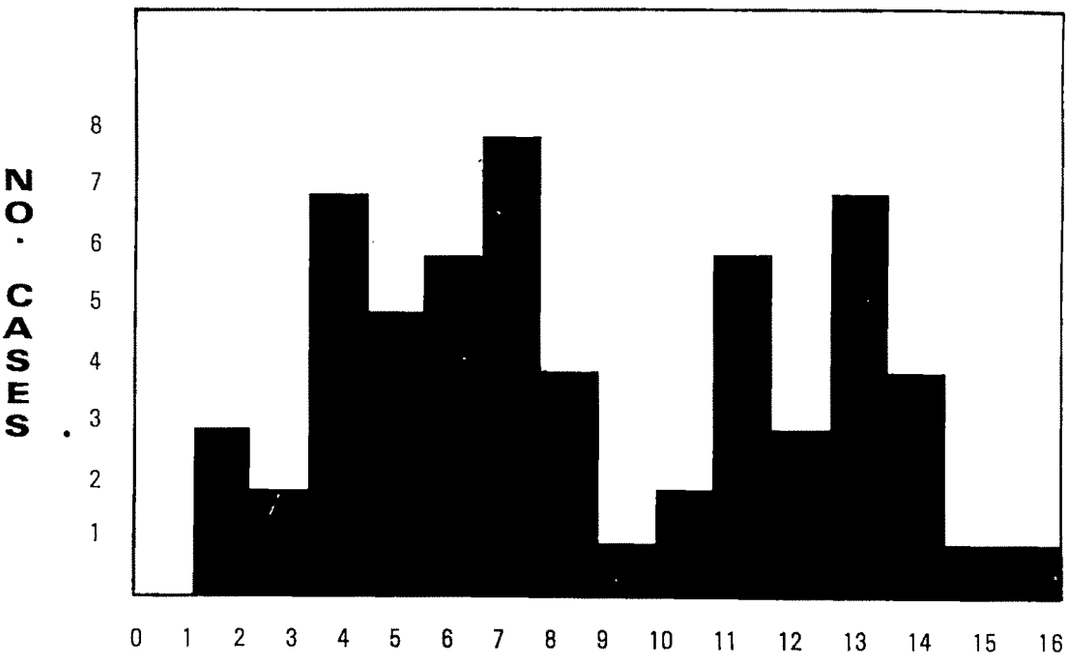


CHART I.

necessarily correlate with the first manifestations of the disease. Each of the lymphocytic group (LC) had a different site of primary involvement: skin, retroperitoneum, groin (lymph nodes), small bowel, parotid gland, and cervical lymph nodes. Of the reticulum cell group, presentations included appendiceal disease, ileocecal bowel disease, ileal disease, a rib lesion and axillary lymph node involvement.

The largest group, lymphoblastic (LB) exhibited the following sites of primary involvement: chest, mediastinum (15); bowel, appendix (1), appendix with liver and spleen involvement (1), ileum and cecum (6), colon and mesentery (2), small bowel (2); stomach (1); lymph nodes, cervical (3), retroperitoneal (5), diffuse (3), mesenteric (1); skin (2); nasopharynx (1); testicle (2); liver (1); liver and spleen (1); tonsil (1); and femur (1).

Clinical findings, signs and symptoms. The clinical findings (Table I) may be suspected by the "primary site of involvement." The most frequent signs and symptoms are listed in Table II.

Leukemic conversion. Nineteen individuals converted from an unequivocal lymphosarcoma state to one of leukemia.

Twelve patients were considered "leukosarcomas" (patients with a lymphosarcomatous mass but who, in addition, had small or moderate degrees of a "positive" peripheral blood or marrow). All of these converted to leukemia during observation or by the time of death.

TABLE I

CLINICAL FINDINGS

Ileocecal mass/or intussusception
Superior vena cava syndrome
Testicular mass
Parotid mass
Skin lesions as a "localized mass"
Fever
Lymphadenopathy
Visceromegaly
Ascites
Masses (primarily lymph nodes)

Eighteen patients showed no conversion to leukemia during the course of the disease and 11 patients either had no follow-up marrow study or did not convert prior to death (without postmortem examination or lost to follow-up). They were also considered "nonconverters." The conversion percentage including the leukosarcoma group was 52. The conversion percentage excluding that group was 40.

Therapy. Surgery, roentgen irradiation and chemotherapy were used alone or in some combination. The surgery included biopsies, resections and palliative procedures (thoracic drainage, colostomy, etc.). Irradiation was by orthovoltage or megavoltage roentgen therapy units.

Chemotherapy included: prednisone, fluoromethalone, cytoxan, vincristine, methotrexate, N-mustards, actinomycin D, 6-MP, asparaginase, cytosine arabinoside, chlorambucil, vinblastine, and allopurinal. The mode of therapy and the combination of therapy are noted in Table III.

Mortality statistics. Five patients are alive. Of these, 3 are without signs or symptoms (at 2, 3 and 13 years); 2 patients of the 5 show evidence of active disease.

Five patients were lost to follow-up examination and are not included in the mortality statistics.

Fifty of the 60 patients are deceased. Of this group 21 patients survived fewer than 6 months, 12 survived from 6 to 12 months, 10 survived 12 to 20 months and 1 survived for 26 months.

Six patients survived more than 26 months and, by standards of duration of survival, 3 of these may have been considered "cures" at one time (actual duration of survival prior to death in these patients was 63 months, 55 months and 39 months). The survival is 9 per cent (5 of 55). The average duration of survival from the time of onset of the disease process was 11 months.

TABLE II

SIGNS AND SYMPTOMS

Bone pain
Weakness
Fatigue
Abdominal pain
Recurrent sore throats
Chronic cough or dyspnea
Weight loss
Abdominal distention
Bowel obstruction
Central nervous system signs

TABLE III

MODE OF THERAPY

Surgery, alone	5
Surgery, roentgen irradiation	6
Surgery, chemotherapy	7
Surgery, chemotherapy, roentgen irradiation	30
Chemotherapy, alone	3
Chemotherapy, roentgen irradiation	8

ROENTGENOGRAPHIC FINDINGS

The occurrence of roentgenographic findings varied considerably. For this reason we have classified them as occurring "very frequently," "frequently" and "infrequently" (occasional).

I. VERY FREQUENT

Anterior mediastinum. The most frequent of all roentgenographic manifestations were those in the mediastinum (18 patients). Of these the anterior mediastinal lesion was noted more often than those in the paratracheal lymph node site (13 of 18). All the mediastinal lesions were lymphoblastic. The thymus was either completely invaded or almost totally replaced by the malignancy. The mass formed exhibits well defined borders and obliterates the retrosternal space (Fig. 1, *A* and *B*).

The superior mediastinal syndrome presented in 5 of the 18 patients. Three of these 5 patients had a paratracheal distribution of mediastinal tumor (see below).

Ileocecal area. Almost as frequent in incidence of roentgenographic presentation are lesions in the ileocecal area of the gastrointestinal tract. These lesions can involve the ileum, ascending colon and appendix, alone or in combination. An in-

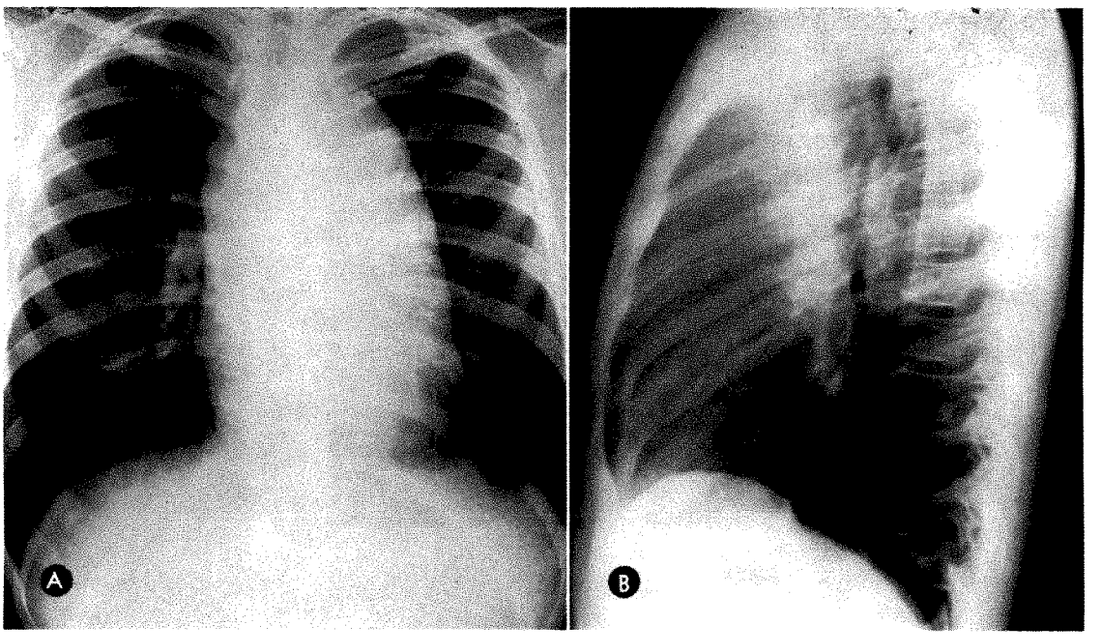


FIG. 1. (*A*) A large retrosternal mass with well defined borders is noted on the posteroanterior chest roentgenogram. (*B*) The position of the mass in the anterior mediastinum is suggested by the opacity anterior to the heart.

tussusception (Fig. 2) is frequently the first manifestation of lesions in this site. The appearance of bowel affected by lymphosarcoma is extremely variable. The clinical and roentgenographic findings most often encountered were palpable or visualized masses, respectively. The mass may displace, invade, or encircle the bowel. A mass need not be apparent; and we frequently noted mucosal effacement, displacement or separation of bowel loops, serosal irregularity with intact mucosa and numerous bizarre patterns.



FIG. 2. The ileum and cecum, invaded with lymphosarcoma, have advanced into the ascending colon creating the classic roentgenographic appearance of an intussusception (arrow).

II. FREQUENT

Paratracheal, mediastinal. In this group we have placed the paratracheal mediastinal lesions. They create symptoms similar to the anterior mediastinal lesions (fatigue, hoarseness, dry hacking cough) and have some roentgenographic features in common. Where the paratracheal lymph nodes are involved or replaced, the mass formed frequently has a well defined border as it abuts on the mediastinal pleura (Fig. 3), similar to the anterior mediastinal lesions. This mass can displace the trachea and compress adjacent vascular structures creating the superior mediastinal syndrome.

Taken as a group, the mediastinal lesions are capable of extension to the pleura (Fig. 4). Frequently a pleural effusion is formed.

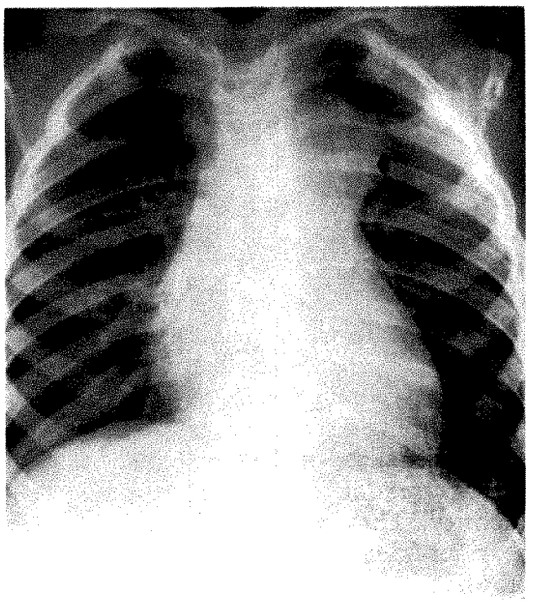


FIG. 3. Lymphosarcoma in the superior mediastinum, but paratracheal (arrow), as opposed to the more frequent presentation in the retrosternal site.

The combination of a mass and an effusion in the chest strongly suggests the diagnosis of lymphosarcoma.

Small bowel and colon. Other manifestations of lymphosarcoma presenting frequently are found in the small bowel and colon. The roentgenographic characteristics of the small bowel lesions have been previously mentioned. That they are bizarre is documented (Fig. 5; 6; and 7). The appearance of diffuse lymphosarcoma of bowel can be mimicked by protein-losing enteropathy, hemorrhage into the bowel wall, malabsorption, sprue, etc. One of our cases did have a protein-losing enteropathy in association with diffuse lymphosarcoma of the small bowel (Fig. 8).

Colon lesions involve the ascending portion more than any other level. Most often this portion of bowel is involved in association with the terminal ileum and appendix. Each may be involved separately, however. Lesions of the colon exhibit a variety of

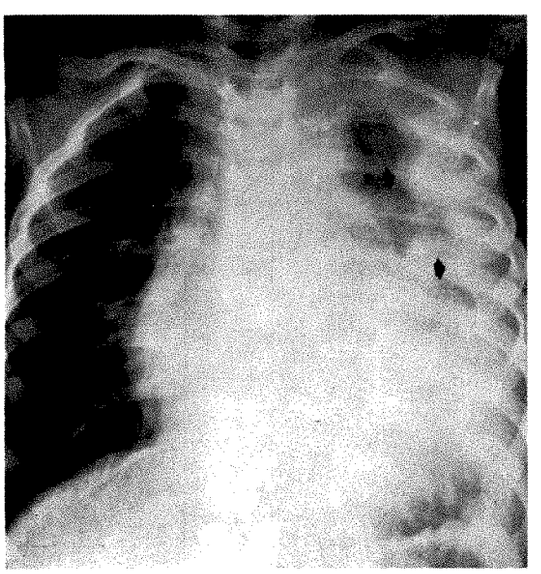


FIG. 4. Masses of lymphosarcoma occupying the pleural space. This appearance is frequently noted after extension of the mediastinal lesions. The masses may become evident only after a pleural effusion has been tapped.

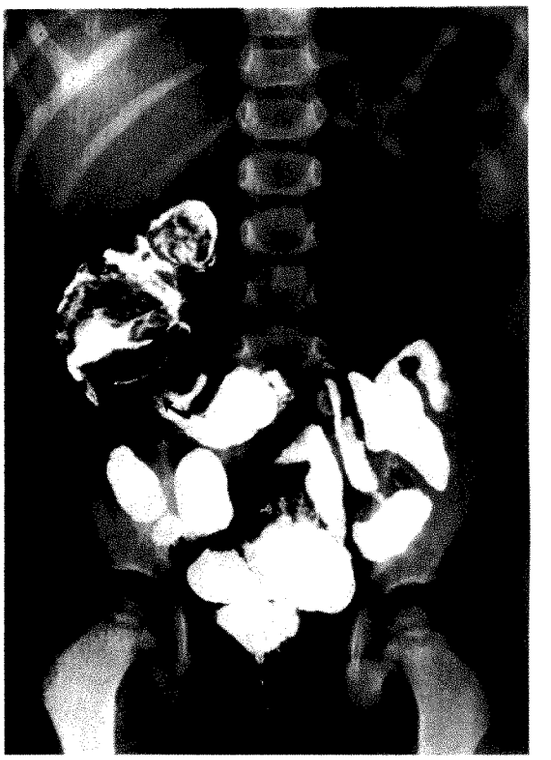


FIG. 5. A delayed roentgenogram obtained during small bowel investigation. The small bowel is diffusely involved. The bowel has lost its mucosal definition and amorphous collections of contrast material are evident. An incidental, nonobstructive, intussusception is demonstrated (curved arrow).

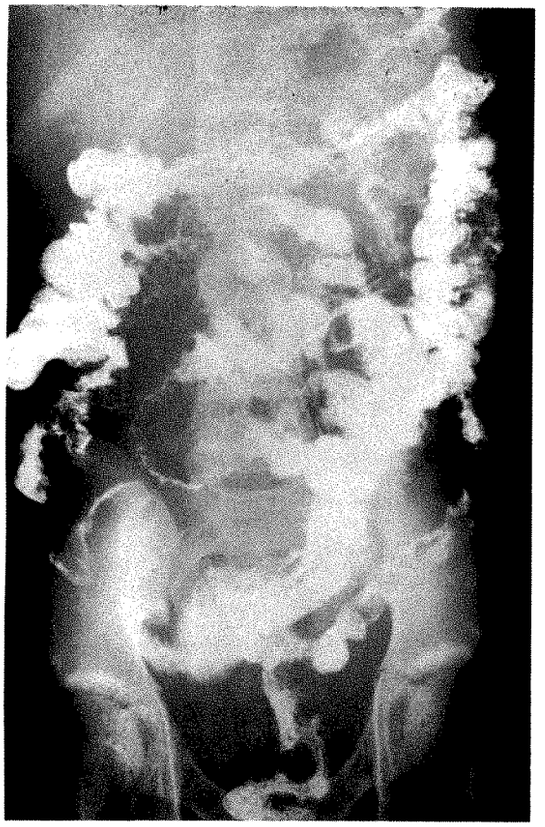


FIG. 6. The mesentery, small and large bowel are diffusely involved with lymphosarcoma. The small bowel loops are separated, narrowed in some areas, and "amorphous" in others. Serial roentgenograms demonstrated many areas to be "fixed."

forms. They can encompass the bowel and create the typical "apple-core" deformity so frequently noted in adults with carcinoma (Fig. 9). They can also produce multiple nodular impressions (Fig. 10), efface long portions of bowel mucosa, giving the colon a denuded appearance (Fig. 11), and cause "thumbprinting" deformities (Fig. 7). Primary colonic lesions were not found beyond the ascending colon. Transverse and descending colon involvement occurred only after extension from other primary bowel or mesenteric foci. The secondary changes are indistinguishable from the primary.

Retroperitoneum. Retroperitoneal disease was suspected because of initial complaints (weight loss with back pain, abdominal pain, etc.) or the finding of a "deep" mass on abdominal palpation. These lesions are demonstrable because of their effect on retroperitoneal structures or on abdominal viscera. The kidneys may be displaced or encompassed (Fig. 12, *A* and *B*) or infiltrated (Fig. 13). These effects may be visualized by intravenous pyelography.

Displacement of the barium-filled stomach or bowel is often noted and helps in localizing the mass lesions.

Liver, spleen. These viscera were involved frequently but only as a part of a more generalized disease process. They were often visualized on a plain abdominal roentgenogram due to their increased size or density. They often displaced juxtaposed barium-filled viscera during examination of the latter.

Bone. An apparent decrease in bone



FIG. 7. Diffuse involvement of small bowel and colon with "fixed" loops of bowel. The bowel is invaded from the mesenteric side in many areas and loops stay separated by the distance noted by the open arrows. The smaller black arrows demonstrate the thumbprinting deformities in the colon.

density ("demineralization") was noted very often; other changes in bone occurred infrequently as a primary roentgenographic manifestation. Bone deformity was not present in association with this frequent characteristic change of demineralization.

III. INFREQUENT

Stomach. The stomach was a primary site of involvement in one child. In this case a "napkin-ring" deformity of the stomach was produced. A large ulcer was noted centrally (Fig. 14). An overhanging edge (sharp cut-off) between the involved and uninvolved portions of the stomach was present. A second child with diffuse intraperitoneal disease also exhibited this finding when the stomach became involved (Fig. 15). Both children died of disseminated disease.

Kidneys, ureters. Although retroperitoneal in location, the kidneys and ureters were not always involved by retroperitoneal lymphosarcoma. Occasionally they were involved primarily. When the kidneys are involved they may be surrounded, infiltrated diffusely, displaced or obstructed. The primary infiltrative form of involvement enlarges the kidneys, sometimes massively and usually bilaterally. Frequently polycystic renal disease is simulated (Fig. 13).

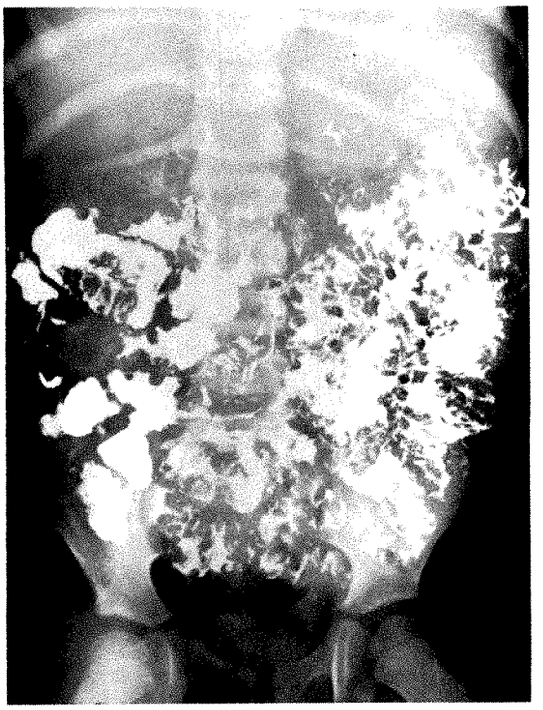


FIG. 8. A picket-fence type deformity of the small bowel suggests a possible protein-losing enteropathy. This patient had diffuse small bowel involvement with lymphosarcoma and a protein-losing enteropathy attributed to the primary disease.



FIG. 9. A circumferential lymphosarcomatous mass has enveloped the ascending colon. The appearance is reminiscent of that seen in adults with carcinoma of the colon.

The ureters were usually displaced when involved. On one occasion the ureter was demonstrated to be narrowed by invasion or compression (Fig. 16).

Bones and joints. Solitary bone lesions (*i.e.*, as the only manifestation of the disease) did not appear in this series. Bone lesions simulating a solitary lesion were noted infrequently (Fig. 17).

Other bone manifestations occurred often during the later course of the disease. These



FIG. 10. Masses of lymphosarcoma have invaded and impressed upon the ascending colon. Recurrence of lymphosarcoma after extirpation of an ileocecal mass can look identical to this image.

included periosteal new bone formation (Fig. 17), translucent bands (Fig. 18) and focal areas of osteolysis (Fig. 19).

Joint manifestations were noted but only as a part of a disseminated disease process. Synovial swelling about the hip joint was present on occasion after dissemination of the disease process (Fig. 19).

IV. MISCELLANEOUS

A number of primary lesions were seen so rarely they were not even classified as "infrequent."

Nasopharynx, tonsils and ethmoids. Lesions in these areas may be observed roentgenographically. A lateral view of the skull and neck did demonstrate abundant "hypertrophic" tissue in the patient with the nasopharyngeal lesion. The one ethmoid lesion extended through the skull base and involved the central nervous system. This was apparent on tomography of the skull base.

Integument. Patients initially presenting with skin lesions manifested roentgenographic changes after dissemination.

Central nervous system. One patient had invasion of the central nervous system from the ethmoids. No primary central nervous system lesion was demonstrated roentgenographically.

DISCUSSION

The age distribution in this report is similar to other large series.[10,16,27] Infrequently a child younger than 1 year of age is reported.[5,29] The peak distribution of ages is between 3 through 7 years and 9 through

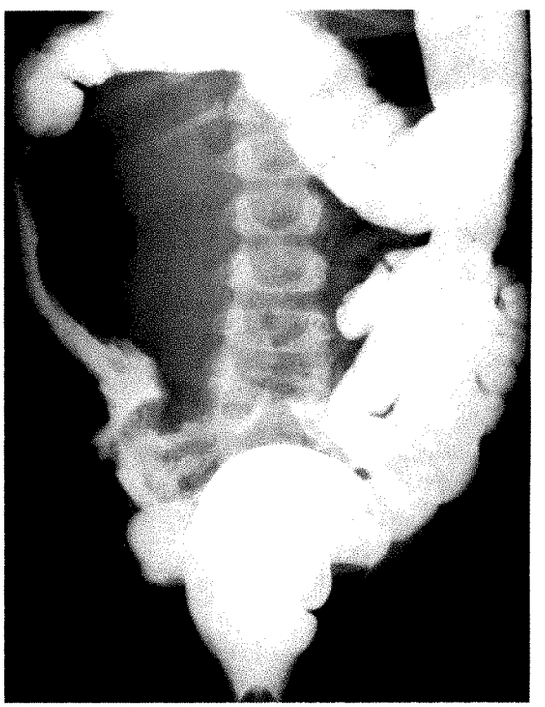


FIG. 11. A large mesenteric mass either arising from, or invading, the ascending colon is present. The ascending limb of the colon appears "denuded" of all layers down to the mucosa.

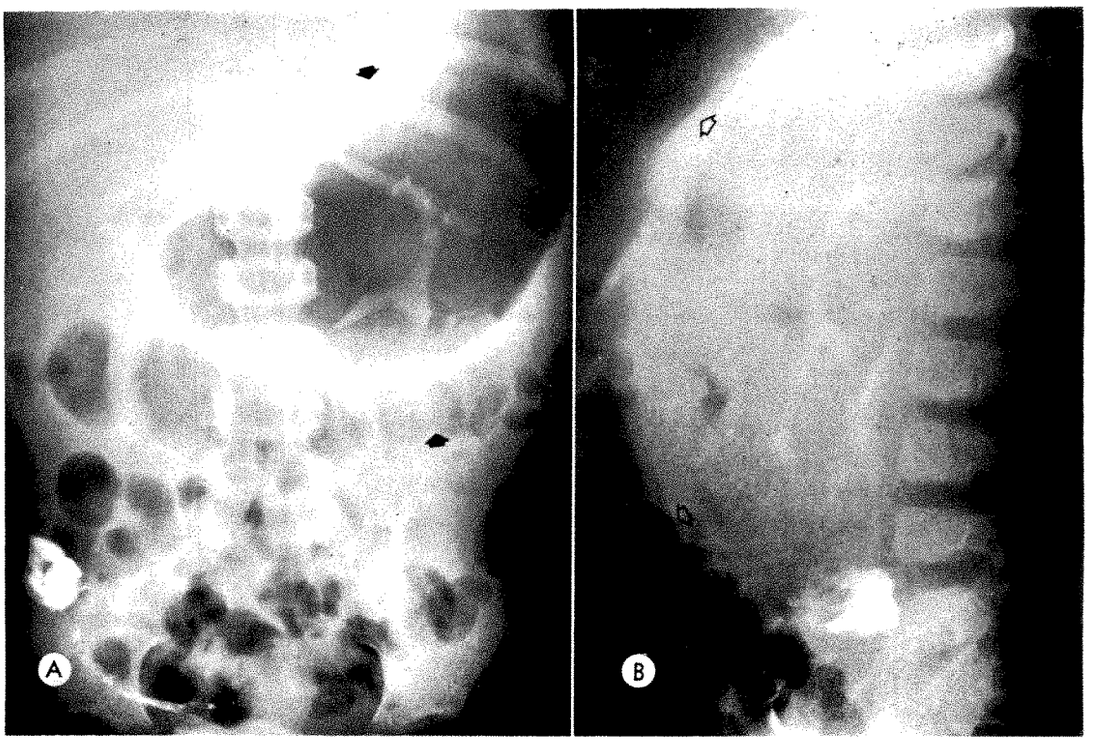
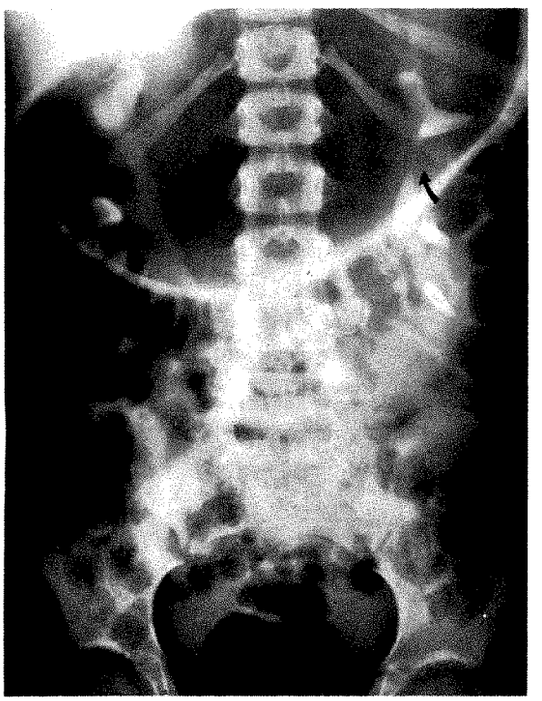


FIG. 12. (*A* and *B*) Intravenous pyelography demonstrates apparent renal enlargement and definite extensive retroperitoneal lymphosarcoma which has surrounded the kidneys (arrows). Although these kidneys were involved, they need not be, even when the retroperitoneal disease is extensive.



14 years. The patient's age should not preclude consideration of lymphosarcoma as a diagnostic possibility. Males were affected between 4 and 5 times more often than females, slightly higher than the figures quoted in other series; but males always predominate.

Classification of lymphomas varies among authors. It is possible to separate Hodgkin's disease because of its characteristic pathologic qualities, but subclassification of the remaining lymphosarcomas is extremely difficult.[2,8,10,13,16,25] No patients with giant

FIG. 13. These kidneys are primarily involved with lymphosarcoma. There is no retroperitoneal disease other than the renal infiltration. The kidneys have assumed the roentgenographic appearance of adult polycystic kidneys—not an infrequent appearance when the kidneys are involved with lymphosarcoma (arrow).



FIG. 14. The body of the stomach is surrounded and invaded by a large primary lymphoblastic lymphosarcoma. The remainder of the patient's clinical and roentgenographic evaluation was normal at this time. Note the sharp borders of the mass and the central ulcer (arrow).

follicular lymphoma were present in this series, but would have been included if any were available for review. Other authors have reported children with giant follicular lymphoma.[2,10,13,24,26,27] This discrepancy may reflect some difficulty in the evaluation of histologic characteristics. Unequivocal classification may not be possible in all instances and it is understandable why the classification of lymphomas is varied and confusing.

Additional difficulty with classification exists because of leukemic transformation of lymphosarcoma and leukosarcomas. It is well known that patients with "pure" lymphosarcomas often develop a leukemic picture. Other patients have a large or evident mass with abnormal cells in the marrow or blood. They are not "pure" lymphosarcoma patients and not leukemic patients,[30] they are considered "leukosarcomas."[14] This series includes patients with a mass and no blood or marrow changes, those with a mass and focal areas of marrow abnormalities and those patients with a large mass and modest amounts of abnormal blood or marrow changes. To the best of our knowledge, they were not leukemia patients.

Close follow-up on our patients enabled documentation of leukemic transformation. Our figures of 40–50 per cent conversion (40 per cent if the leukosarcoma group is excluded) are consistent with other large series.[16,28] The clinical presentations vary so considerably that an attempt to categorize



FIG. 15. The stomach in this child was involved after a known lymphosarcomatous process in the peritoneal cavity had spread to the gastric wall. Note that sharp borders of the mass are demonstrated in this "secondary" gastric involvement just as they were in the primary type of invasion (arrow).

them would necessarily include any finding associated with the innumerable complaints of an ill child. Some complaints are voiced more frequently than others because the occurrence of lymphosarcoma at some sites is greater than others. Thus the common complaints most often are referable to the chest (dry hacking cough) and the abdomen ("belly-ache").

The success of various forms of therapy is not the primary consideration of this report. The mortality statistics indicate that curative therapy for most lymphosarcoma patients is unavailable. Therapy which did affect a "cure" (greater than 5 years without recurrence) was no different from the therapy given to those who died of their disease. The greatest effect of treatment was palliation. There are reviews of specific therapy in the literature,[10,24,25,27] and it is not within the scope of this paper to include a further discussion of it.

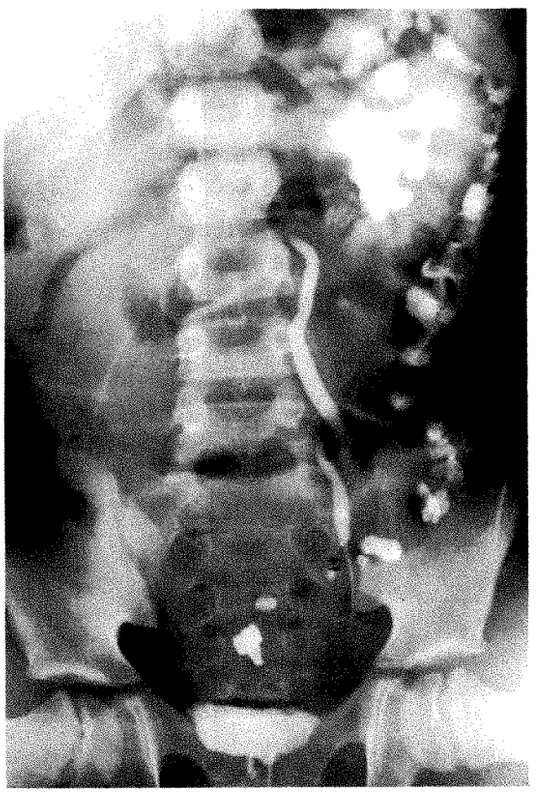


FIG. 16. The distal ureter is narrowed in this patient with retroperitoneal disease (arrows). Compromise of the ureter is seldom noted with lymphosarcomatous disease and patients seldom succumb due to renal failure.

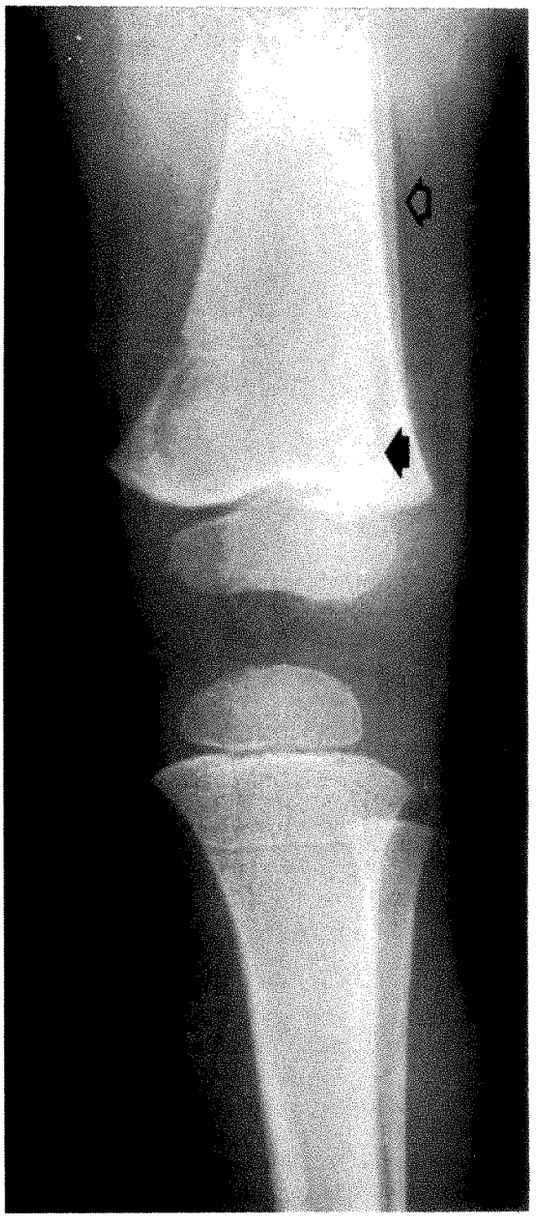


FIG. 17. An apparent solitary cystic destructive lesion in the distal femur (black arrow). Although this was the first site of disease discovered, the patient had other evidence of disseminated lymphosarcoma at this time. Periosteal bone reaction is evident (open arrow).

The survival rate in this series is at the

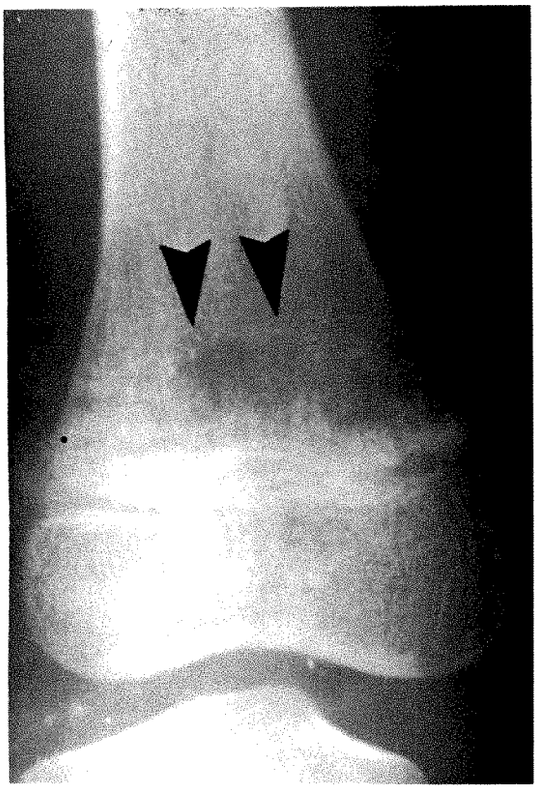


FIG. 18. Translucent bands (arrows) were noted on occasion in patients with and without disseminated disease. This patient had no disseminated disease at the time the roentgenograms were obtained.

low end of survival statistics noted in the literature (8 to 30 per cent 5 year survival).[2,10,15,16,24,25] Some discrepancy may be due to inclusion of giant follicular lymphoma cases in those series which have notably long survivors.

The roentgenographic findings are as bizarre and varied as the clinical signs and symptoms. This is due to the almost protean nature of the disease. Those manifestations of lymphosarcoma which present repeatedly, however, frequently exhibit similarities from patient to patient. This is especially true of the mediastinal lesions and lesions about and in the ileocecal area of the gastrointestinal tract.

The superior mediastinal syndrome occurred frequently in the patients with mediastinal disease. This is an unusual phenomenon in children with all forms of cancer,[9] but not in children with lymphosarcoma if they are considered as a special group.

Lymphosarcomas involving the region of the distal ileum and cecum predispose the patient to an intussusception. Generally the lymphosarcoma arises in the lymphoid follicles of the submucosal layer of bowel.[8] From this site it can proliferate into a locally large mass, form multiple polypoid masses, or invade mesentery, serosa or mucosa. Thus, a varied number of roentgenographic appearances may be observed.[22] The lesion seldom causes obstruction unless associated with an intussusception. The latter occurs very frequently (33 per cent of this series) and approaches 50 per cent or more of the reported cases when the small bowel is involved.[1,11,18]

Our impression of the outstanding feature of the lesion in the small bowel and involving the ileocecal area is the roentgen evidence of a mass or masses. It may be local or multifocal with the association of impression and displacement or invasion of bowel.

Cures from extirpation of a mass in the ileocecal area have been reported.[5,11–13]

The retroperitoneum is involved frequently,[15,16] but does not necessarily manifest itself early roentgenographically. It can be involved as part of a generalized disease

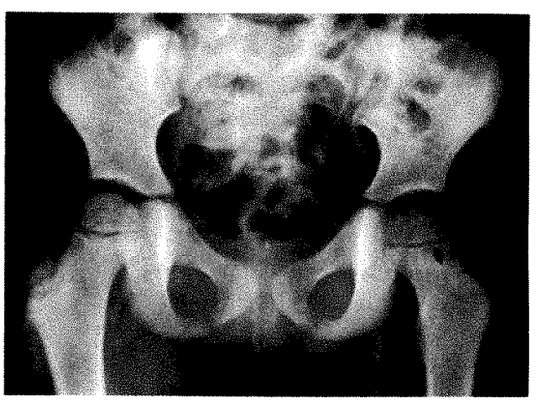


FIG. 19. The pelvis of a child with hip pain. A destructive lesion of the proximal femur is evident (dark arrow). Also demonstrated is synovial thickening (open arrow) which is noted in patients with benign synovitis. In patients with lymphosarcoma we noted this finding only in patients who had converted to leukemia.

process (and frequently is), and other findings (visceromegaly, cervical, inguinal or generalized lymphadenopathy) may be cause to suspect the presence of disease in the retroperitoneum.

The retroperitoneal lesions can be investigated by routine studies, including intravenous pyelography, stomach and small bowel, and barium enema examinations. Oblique and lateral projections are very helpful for defining the course of the ureters and position of the retroperitoneal portions of the colon more accurately. Manifestations of retroperitoneal disease occur frequently in association with more obvious sites of disease and the lesion is generally large at the time initially palpated. Biopsy of lymph nodes or surgery in an attempt to remove the retroperitoneal mass yields the diagnosis and lymphangiography is seldom necessary.

The liver and spleen are frequent sites of involvement;[15,24,28] however, evidence of disease in those sites is usually apparent from clinical investigation or by observation of the plain abdominal roentgenogram. No special roentgenographic techniques for evaluation of these viscera were necessary.

We have classified bone manifestations as occurring frequently and infrequently. "Demineralization" of bone may be produced by the catabolic state created by the disease and/or therapy. It can also be caused by tumor replacement of marrow.

The effect of lymphosarcoma on bone is seldom the first manifestation of the disease, but late in the disease almost any form of bone reaction can be present.

Examination of the pathology of renal disease has shown a focal and sometimes massive loss of general corticomedullary architecture by diffuse infiltration of tumor through cortex, glomeruli and tubules.[23] This may suggest the reason for poor roentgenographic demonstration of the calyceal system during intravenous pyelography. When poor visualization occurs, we inject additional contrast material and obtain delayed roentgenograms. On occasion these techniques have been successful when the routine study was inadequate.

We have indicated a group of lesions as occurring sporadically and placed them in a miscellaneous category. The literature (primarily those reporting clinical data) suggests that some of these sites are frequently involved.[2,10,15,16,24,25] The discrepancy is due to the fact that we have attempted to emphasize the first roentgenographic manifestations of the disease. This group of lesions includes lesions of the nasopharynx, tonsils, ethmoids, integument, central nervous system, gonads and parotid glands.

Some special techniques may be of value in defining the nature or extent of these lesions. Lateral views of the head and neck will aid in defining the presence of lymphosarcoma in the pharynx or retropharynx. Tomography through the base of the skull is useful because it helps to demonstrate the presence or absence of destruction of the skull base due to invasive disease arising in the pharynx or paranasal sinuses.

SUMMARY

Lymphosarcoma in children represents about 10 per cent of the malignant neoplasms found in the pediatric age group. It is found more often in males and seldom under 1 year of age.

Classification is difficult, but most lesions can be classified as lymphoblastic, lymphocytic, or reticulum cell sarcomas.

Conversion of lymphosarcoma to leukemia is frequent (one-third to one-half of reported cases) and survival is low. Cures are reported, however.

The initial sites of involvement determined clinically and defined roentgenographically are not necessarily identical, but both suggest that the most frequent sites of primary involvement are the mediastinum, gastrointestinal tract, retroperitoneum and lymph nodes (diffusely).

Initial roentgenographic findings may be considered as occurring very frequently, frequently, or infrequently (occasionally).

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RADIATION HEPATITIS INDUCED BY ABDOMINAL IRRADIATION WITH THE COBALT 60 MOVING STRIP TECHNIQUE*

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SINCE carcinoma of the ovary may implant on any peritoneal surface, treatment of the entire abdominal cavity is required for patients with ovarian cancer who receive postoperative irradiation. Radiation therapy following surgical excision is effective in properly selected patients with the common epithelial cancers of the ovary.

Treatment of the entire abdomen by the so-called "moving strip" technique has been commonly used at The University of Texas M. D. Anderson Hospital and Tumor Institute in Houston, Texas for postoperative therapy for these patients. We have found that it is necessary to shield a portion of the liver with 1 half-value layer of lead or irreversible liver damage may result. In our experience of 65 patients treated without protecting the liver, 14 developed radiation hepatitis.

MATERIAL AND METHOD

The moving strip technique was adapted to a cobalt 60 teletherapy unit.[2] The abdomen and back were divided into continuous segments or "strips" of 2.5 cm. A single strip of 2.5 cm. was treated on the first day from the front, and on the second day an identical opposing field was irradiated from the back. The treatment field was increased by 1 strip every day until 4 strips (10 cm.) were being treated. The 10 cm. segment was moved up 2.5 cm. every day until the last strip reached the dome of the diaphragm. The field was then reduced progressively by 1 strip (2.5 cm.) each day, and on the last 2 days of treatment, a single 2.5 cm. strip was irradiated. Prior to 1965 the liver was not shielded, but the entire liver was not in the full dose zone. The kidneys were shielded from the posterior fields by 2 half-value layers of lead.

In 1965 the treatment technique was changed to include the liver in the radiation field because a young patient with dysgerminoma of the ovary developed a single recurrence of the tumor on the dome of the liver, thus demonstrating a region not adequately treated and suggesting a possible site for failure in all patients receiving irradiation. Therefore, for the 32 months of this study, all patients received the full dose of irradiation to the entire liver. This required adding 2 strips (5 cm.) to our regular treatment field.

There were 65 patients with ovarian cancer treated by this technique in the period January 1965 to August 1967. The doses ranged from 2,450 to 2,920 rads in 12 days (2½ weeks). The treatments were generally well tolerated, but varying degrees of nausea, vomiting, diarrhea, and bone marrow depression occasionally resulted. These problems, when encountered, resolved with only brief interruptions in the treatment schedule.

Fourteen of the 65 patients were apparently cured of cancer and were noted to have had clinical findings of radiation hepatitis. Eleven of the 14 died either directly or indirectly as a result of the radiation injury. None of the patients had a history of previous liver disease and only 1 (Patient 14) had received prior chemotherapy.

Based primarily on the time of appear-

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ance of symptoms, patient survival, and, to some degree, on histologic changes, the patients can be separated into 3 groups:

Group I (acute form) comprised patients who developed evidence of hepatic injury 4 to 24 weeks following completion of radiation therapy (Table I). All had ascites and/or pleural effusions. Laboratory evidence of liver injury included an elevation of serum alkaline phosphatase and bromsulfphalein (BSP) retention at 45 minutes. Five of the 8 patients with acute injury died within 10 months following completion of therapy. Two patients had an exploratory laparotomy because of the findings of ascites which suggested recurrent carcinoma of the ovary. Their postoperative courses were complicated by further hepatic decompensation due to the stress of surgery.

Group II (subacute type) consisted of patients who developed ascites 8 to 28 weeks following completion of radiation therapy and partial recovery (Table II). The symptoms during the interval between

TABLE I

TREATMENT AND CLINICAL DATA FOR RADIATION HEPATITIS PATIENTS

GROUP I

Patient	Liver Dose (rads)	Symptoms	Onset of Symptoms After Completing Therapy	Survival After Completion of Therapy	Comment
1	2,689	Ascites	4 wk.	3 mo.	Liver failure main cause of death
2	2,913	Ascites; pleural effusion	8 wk.	9 mo.	Fluid, electrolyte problem, rapid deterioration, abnormal liver function studies
3	2,540	Ascites; pleural effusion; hepatomegaly	6 wk.	7 mo.	Clinical picture of liver failure due to veno-occlusive disorder
4*	2,600	Ascites	6 wk.	6 mo.	Exploratory laparotomy revealed necrosis of left lobe of liver; died postoperatively with liver failure
5	2,486	Ascites	20 wk.	10 mo.	Exploratory laparotomy for ascites (no cancer); developed immediate postoperative anasarca fluid, electrolyte imbalance and progressive deterioration
6	2,452	Ascites	7 wk.	Died	Mild involvement; no residual liver impairment; died due to lung carcinoma
7	2,650	Ascites	24 wk.	Living and well	Exploratory laparotomy for small bowel obstruction; postoperative liver impairment but recovered
8	2,692	Ascites: hepatomegaly; pleural effusion	8 wk.	Living and well	Effusions regressed with clinical and laboratory improvement over 12 month interval

* Received an additional 2,000 rads to the paraaortic lymph nodes (8×12 cm. field).

TABLE II

TREATMENT AND CLINICAL DATA FOR RADIATION HEPATITIS PATIENTS
GROUP II

Patient	Liver Dose (rads)	Symptoms	Onset of Symptoms After Completing Therapy	Survival After Completion of Therapy	Comment
9	2,550	Ascites	8 wk.	18 mo.	Exploratory laparotomy for bowel perforation and peritonitis; died 4 months later; liver failure a contributing factor
10	2,620	Ascites	12 wk.	20 mo.	Exploratory laparotomy 12 weeks post-therapy for ascites (no cancer); developed immediate postoperative fluid and electrolyte imbalance; experienced progressive deterioration and 1 year later died
11	2,699	Ascites	12 wk.	23 mo.	Evidence of radiation hepatitis early; died due to unknown causes
12	2,767	Ascites; pleural effusion	7 mo.	37 mo.	Developed ascites and was placed on chemotherapy; however, did poorly and sent to nursing home; returned 2 years later in congestive heart failure with ascites and pleural effusion

the acute manifestations and death were of variable severity. In 3 of the patients, hepatic insufficiency was well documented (Patients 9; 10; and 12). The fourth patient (Patient 11) was started on Alkeran because the ascites was thought to represent recurrent cancer. She continued to deteriorate and died in a cachectic state without evidence of cancer. In retrospect, her clinical picture was that of chronic liver insufficiency.

Group III (chronic type) contained the patients who developed hepatic insufficiency 24 and 39 months after completing therapy (Table III). These patients exhibited clinical and histologic evidence of

TABLE III

TREATMENT AND CLINICAL DATA FOR RADIATION HEPATITIS PATIENTS
GROUP III

Patient	Liver Dose (rads)	Symptoms	Onset of Symptoms After Completing Therapy	Survival After Completion of Therapy	Comment
13	2,624	Ascites; pleural effusion	24 mo.	29 mo.	Sudden onset of refractory congestive heart failure, ascites, pleural effusion and death
14	2,920	Ascites; pleural effusion	39 mo.	44 mo.	Exploratory laparotomy for ascites revealed a small liver (no cancer); progressive liver decompensation produced death 5 months later

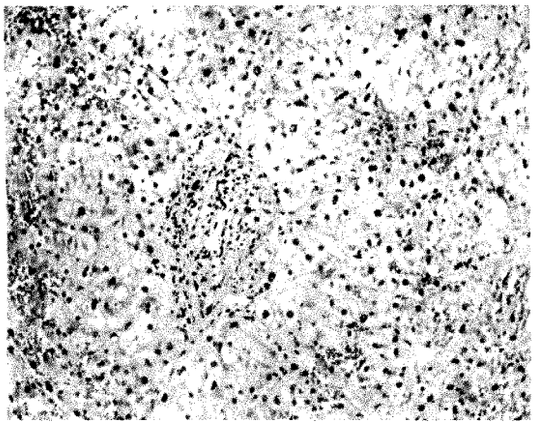


FIG. 1. Patient 3. Fibrous occlusion of the central vein, mild fatty change in the liver cells, and moderate congestion in the peripheral portion of the lobule noted 94 days after completion of irradiation. Hematoxylin and eosin (×100).

liver injury. One patient (Patient 13) died after a 5 month history of anasarca, congestive heart failure, and altered liver function. She had been symptom-free for 2 years.

REPORT OF CASES

GROUP I

PATIENT 3. This 59 year old housewife had an 8 cm. ovarian carcinoma (Stage II-B) which was adherent to the pelvic wall. She received postoperative irradiation to the entire abdomen by the moving strip technique. The liver received 2,540 rads. Six weeks after completing treatment, she developed ascites, pleural effusion, and hepatomegaly.

Liver chemistry analyses showed: alkaline phosphatase of 8.9 Bessey-Lowry units (normal 0.8 to 2.3 units); serum glutamic pyruvic transaminase (SGPT) 34 units (normal 0–35 units); serum albumin 2.8 gm. per cent; total bilirubin 0.2 mg. per cent; and 48 per cent BSP retention after 45 minutes. A percutaneous needle biopsy 94 days after completing therapy showed moderate congestion, occlusion of the central vein, and atrophy of liver cords (Fig. 1).

The patient's condition deteriorated and she died from liver failure 7 months after completing irradiation. The clinical situation was similar to that seen with veno-occlusive disease of the liver. The immediate cause of death was hematemesis.

PATIENT 2. This 50 year old housewife had a bilateral salpingo-oophorectomy and partial omentectomy for a Stage III serous carcinoma of the ovary. She received postoperative irradiation by the moving strip technique. The liver received 2,913 rads. Eight weeks after completion of her treatment, she developed ascites and pleural effusion. The BSP retention was 32 per cent after 45 minutes. Cytologic analysis of the ascitic fluid revealed no malignant tumor cells. The patient experienced increasing hepatic dysfunction and died 9 months after completing her irradiation.

GROUP II

PATIENT 10. This 52 year old patient had a right salpingo-oophorectomy for a Stage II carcinoma of the ovary. She was referred immediately to M. D. Anderson Hospital, and a total abdominal hysterectomy and left salpingo-oophorectomy were done. The abdomen was irradiated; the liver received 2,620 rads.

The patient developed ascites 12 weeks later. An exploratory laparotomy revealed no evidence of cancer and the liver was biopsied. Preoperative laboratory values were as follows: alkaline phosphatase 3.4 Bessey-Lowry units; 10 per cent BSP retention at 45 minutes; total bilirubin 0.5 mg. per cent; and SGPT 17 units. The liver histologic study revealed periportal fibrosis, hyaline thickening of the arterial walls (Fig. 2), and subintimal thickening and occlusion of the central veins (Fig. 3).

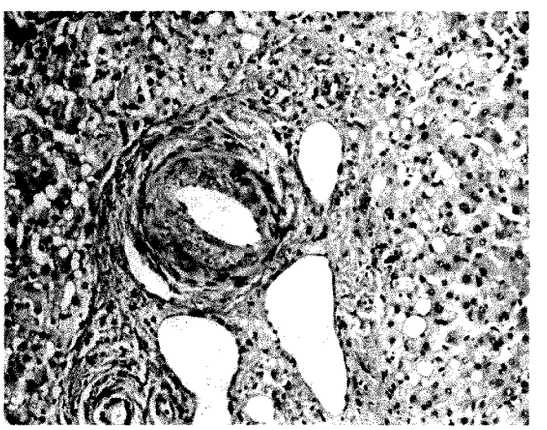


FIG. 2. Patient 10. Fibrosis surrounds all structures in the portal triad, and subintimal fibrous thickening of a hepatic artery branch is pronounced (90 days after irradiation). Hematoxylin and eosin (×100).

During the immediate postoperative period, she experienced edema, ascites, and congestive heart failure. She died 14 months later. During the interval from surgery until death she was unable to maintain her nutritional status and was confined to her home.

Patient 12. This 63 year old woman had a total abdominal hysterectomy and bilateral salpingo-oophorectomy for a Stage III ovarian carcinoma on March 4, 1965. The liver received 2,767 rads. Ascites and bilateral pleural effusion appeared 7 months later, and the patient was started on L-phenylalanine mustard. After 4 courses of chemotherapy, she was thought to have advancing disease and was sent to a nursing home for terminal care.

On April 17, 1967 (almost 2 years later) she was readmitted to M. D. Anderson Hospital with ascites, pleural effusion, and fluid and electrolyte imbalance, and died. Laboratory examinations included an alkaline phosphatase of 3.4 Bessey-Lowry units, total bilirubin 0.7 mg. per cent, serum albumin 3.4 gm. per cent, and SGPT 22 units. The postmortem examination revealed no evidence of malignancy. The histologic findings in the liver were periportal fibrosis, subintimal fibrosis of the portal veins and subintimal fibrosis and occlusion of the central veins (Fig. 4).

GROUP III

Patient 14. This 43 year old housewife developed ascites, and an exploratory laparotomy revealed inoperable Stage III carcinoma of the ovary. After operation, she was referred to M. D. Anderson Hospital where she was started on Alkeran, 1 mg./kg. body weight, in divided doses over 5 days every 4 weeks. She received 5 courses of Alkeran over a 5 month interval, with almost complete regression of her tumor. Because of the excellent response of her tumor to chemotherapy, she was given a so-called "second look" procedure with a total abdominal hysterectomy and bilateral salpingo-oophorectomy and removal of tumor implants from the pelvic peritoneum. The liver was free of metastatic cancer and appeared normal. She received postoperative irradiation by the moving strip technique. The liver received 2,920 rads. The therapy was completed on September 13, 1965.

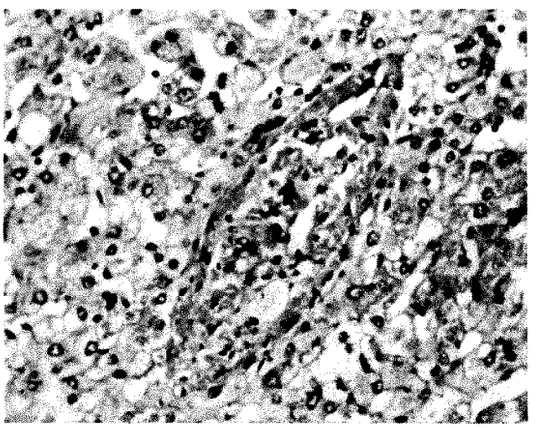


Fig. 3. Patient 10. A dilated and occluded efferent vein with small spaces lined by epithelial cells suggesting recanalization within a fibrous core 90 days after irradiation. Hematoxylin and eosin (×200).

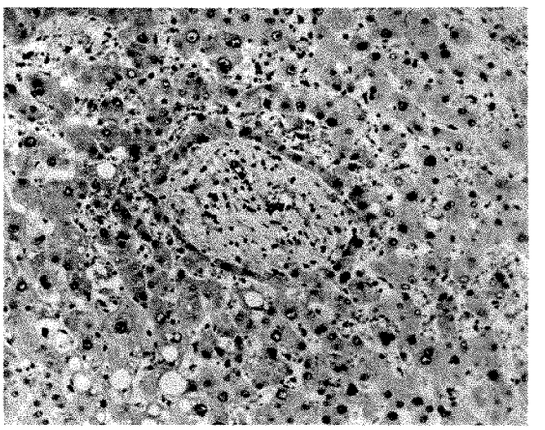


Fig. 4. Patient 12. Dense fibrotic obliteration of the hepatic vein 37 months after completion of irradiation of the liver. Hematoxylin and eosin (×100).

The patient remained asymptomatic until January, 1969, when she developed ascites. Liver damage was suggested by a 60 per cent BSP retention after 45 minutes, and an alkaline phosphatase of 3.7 Bessey-Lowry units. However, the SGOT was 85 units, serum albumin 3 gm. per cent, and total bilirubin, 1 mg. per cent. The patient was explored because of suspected recurrent cancer on January 22, 1969, and a small, shrunken liver was noted. Multiple biopsies from the abdominal cavity revealed no evidence of residual neoplasm. The postoperative course was complicated by sepsis, ascites, and edema. Numerous laboratory studies consistently revealed a low serum albumin, normal or slightly elevated SGOT, slight elevation of bilirubin, and significant BSP retention after 45 minutes (76 per cent on February 4, 1969). A

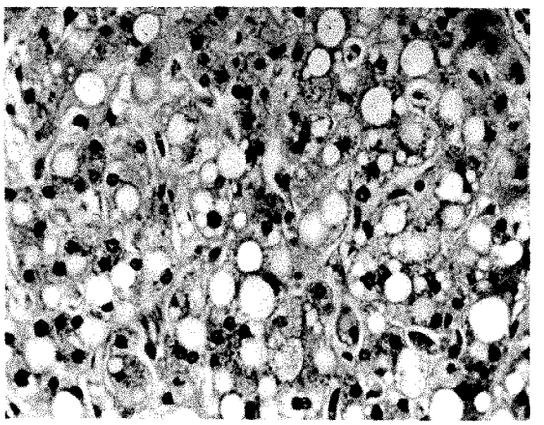


FIG. 5. Patient 14. Severe fatty metamorphosis and granular degeneration in the parenchymal cells were present in all sections examined (Fig. 5, 6, and 7, 39 months after irradiation). Hematoxylin and eosin (×200).

liver biopsy at the time of exploration revealed evidence of hepatic parenchymal atrophy, fatty metamorphosis, centrilobular congestion, and fibrin deposits in the central veins (Fig. 5; 6; and 7).

The patient died April 29, 1969 from hepatic insufficiency.

DISCUSSION

The intolerance of the liver to irradiation is now quite clear.[1,3–7] Ogata *et al.*[5] described pathologic changes in the hepatic vessels of livers partially included in the treatment fields of patients receiving irradiation for lung cancer. The lumina of the small hepatic veins were occluded by subintimal fibrous thickening, and it was suggested that the vascular lesions were a direct result of irradiation.

Ingold *et al.*[3] were the first to describe the clinical aspects of radiation hepatitis. They reported 13 cases caused by irradiating the entire liver. The doses, given by the open field method, ranged from 1,300 rads in 18 days to 5,100 rads in 40 days. The median dose was 3,900 rads. In patients with radiation injury, characteristic manifestations appeared within 2 to 6 weeks following completion of radiation therapy to the liver. The patients developed ascites and enlarged livers. The results of function studies were abnormal; elevated serum alkaline phosphatase was the most frequent laboratory finding. Three of the 13 patients died as a result of radiation injury. Reed and Cox[6] studied these cases and reported that the irradiation had caused diminution in size and number of hepatic cells and progressive fibrosis and obliteration of the hepatic venous radicals, producing a type of veno-occlusive disease. However, in those patients who survived more than 4 months, there was evidence of re-establishment of competent hepatic circulation and return of hepatic structure toward normal.

Irradiation of the entire liver by the

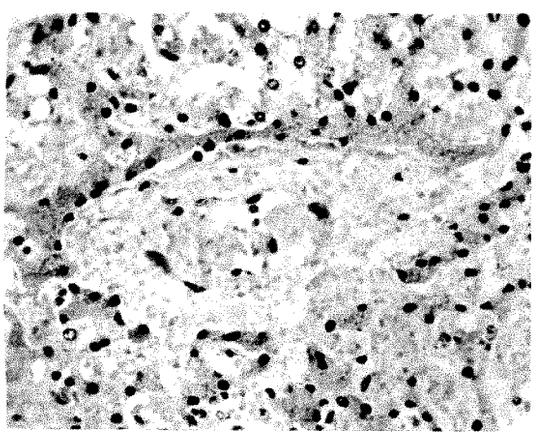


FIG. 6. Patient 14. A dilated efferent vein is occluded by a fibrin thrombus. Hematoxylin and eosin (×200).

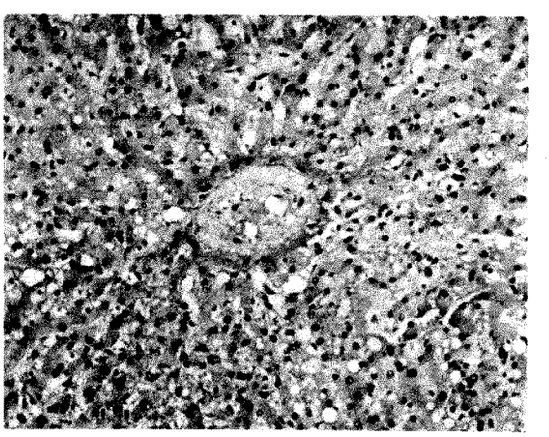


FIG. 7. Patient 14. A central vein occluded by dense fibrous tissue. Hematoxylin and eosin (×100).

moving strip technique may cause irreversible hepatic damage. The onset of symptoms and the survival are variable, but suggest an acute, subacute, and chronic type of injury. In all 3 groups the patients developed peritoneal and/or pleural effusions and altered liver function. The relationship of the pleural effusion to hepatic dysfunction is unclear, since patients with portal hypertension due to hepatic vein occlusion selectively accumulate fluid in the peritoneal cavity. Hypoalbuminemia could possibly contribute to the collection of fluid in the pleural spaces.

Seven patients were given L-phenylalanine mustard (Alkeran) before death because their ascites was thought to represent recurrent cancer. It is doubtful that this medication played any part in the hepatic failure experienced by the patients. Nor was metastatic cancer a factor, for 9 patients of the 14 had an exploratory laparotomy or autopsy and only 1 had evidence of cancer (nodule in the omentum).

The histologic changes in irradiated livers are variable, depending upon the severity of the injury and the length of time between exposure and obtaining a specimen. Changes in the central veins are the most consistent observation. Subintimal fibrous thickening of the vein wall is apparently an early phenomenon and is rapidly followed by deposition of fibrin in the venous lumina, leading ultimately to occlusion. The thrombus rapidly organizes, resulting in the formation of circumscribed fibrous nodules in lobular centers. Within these, fine capillaries presumably representing recanalization can be seen. Concomitantly, there is congestion of the sinusoids, most intense near centers of lobules, and subsequent atrophy of liver cords. In late cases, the structures of the portal areas also show fibrosis. This is usually most intense around the portal vein radical, but spreads out through the triad region, enveloping both hepatic artery and bile duct. The intensity of the venous changes is usually moderately variable from focus to focus within the same specimen. It is clear, from clinical data, that at least some of these pathologic changes are reversible. The exact sequence of events, however, is too poorly known to permit an estimate of the stage at which the point of irreversibility is reached.

The diagnosis of radiation hepatitis was made prior to death in some of these patients. The usual treatment for liver disease, such as high caloric diet, salt restriction, rest, and diuretics, was not successful except in 3 patients with mild impairment. Two of these patients are alive more than 5 years, and have no evidence of abnormal liver function. The patients frequently developed refractory congestive heart failure; this can be expected in management of severe injuries.

A safe dose to the entire liver using the moving strip technique has not been determined. Ingold *et al.*[3] stated that 3,000–3,500 rads in 3 to 4 weeks using the open field technique is a safe dose.

At the present time at M. D. Anderson Hospital, the dome of the liver is shielded with 1 half-value layer of lead. A portion of the liver receives 2,600–2,800 rads, and no evidence of liver injury has been noted (Fig. 8).

SUMMARY AND CONCLUSIONS

1. Irradiation of the entire liver with doses of 2,450 to 2,920 rads given by the moving strip technique caused liver injury in 14 of 65 patients treated.

2. The clinical picture of radiation hepatitis may consist of hepatomegaly, ascites, pleural effusion, and alteration in liver function. The response to the injury sustained is variable, and patients may die within a short time (Group I). The chronic form may be a continuation of the acute injury (Group II), or the patient may experience an abrupt onset of symptoms (Group III).

3. Sinusoidal congestion, parenchymal atrophy, and subintimal fibrous thickening of the central veins are early histologic manifestations of liver injury, whereas

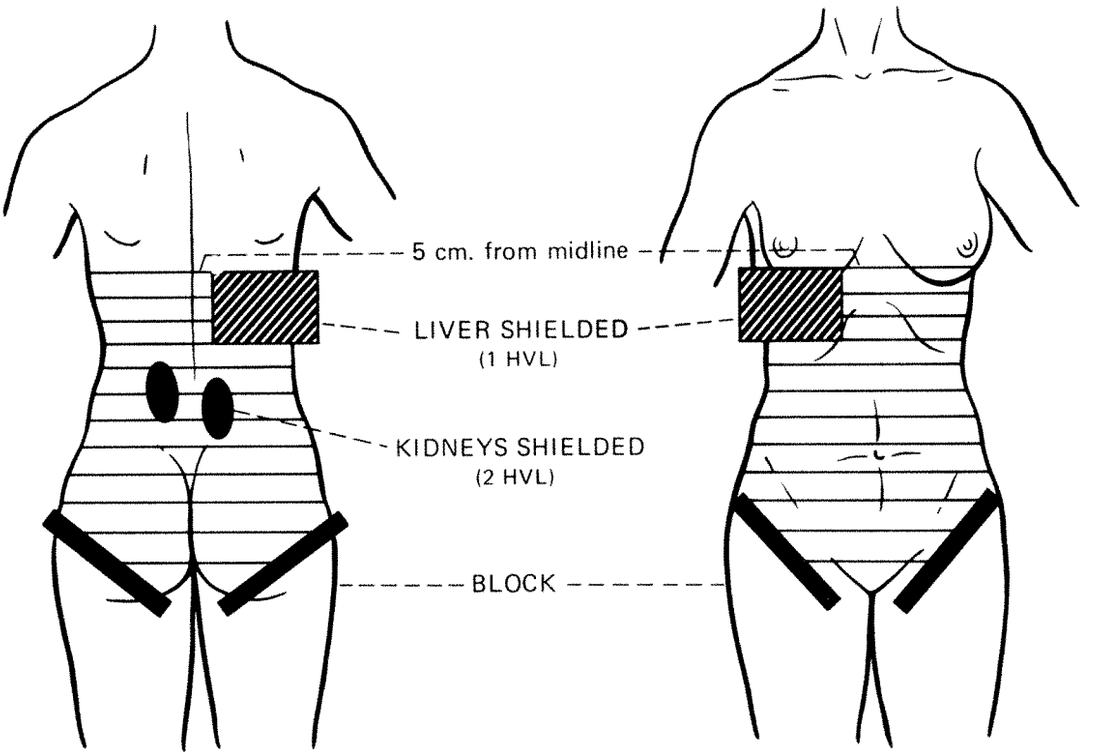


FIG. 8. Volume covered with the megavoltage moving strip technique.

The kidneys are shielded from the posterior beam by 2 HVL of lead placed on a satellite platform (this will reduce the dose to the kidneys to about 50 per cent of the tumor dose). The right side of the liver (3 strips) is shielded both front and back with 1 HVL of lead. (Courtesy: Fletcher, G. H. Textbook of Radiotherapy. Second edition. Lea and Febiger, Philadelphia.)

dense fibrous occlusion of the vein lumina is a late effect.

4. A safe dose to the entire liver with the moving strip technique has not been determined. Part of the liver is no longer included in the treatment field.

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PRIMARY PLASMOCYTOMA OF THE SPLEEN*

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PRIMARY tumors of the spleen are uncommon. This is true both of benign and malignant tumors. Malignant tumors of the spleen usually belong to the groups originating from the lymphatic or reticuloendothelial system.[4] Hemangiosarcomas are also sometimes encountered. Benign splenic tumors usually are fibromas, hemangiomas, hamartomas or cysts of different nature.[4]

Primary plasmocytoma of the spleen has, to my knowledge, not been reported in the radiologic literature before. Recently we examined a patient with a splenic tumor that proved to be a solitary plasmocytoma.

This report deals with the roentgenographic findings mainly, as the case has previously been discussed elsewhere from a clinical point of view.[7]

REPORT OF A CASE

This 29 year old male was admitted with slight fatigue of a few months' duration, and an erythrocyte sedimentation rate of 107 mm. Physical examination revealed no definite abnormalities. The spleen could not be palpated with certainty. Peripheral blood smear and bone marrow smears were both normal; in particular, there was no increase in plasma cells. Total serum proteins were somewhat elevated, 10.1 gm./100 ml. (normal 6.5–8). Serum electrophoresis showed, however, a marked increase in gamma-globulins amounting to 5.2 gm. 100 ml. (normal 0.9–1.7).

Intravenous urography revealed an enlarged spleen displacing the left kidney downward. Otherwise the kidneys were normal (Fig.

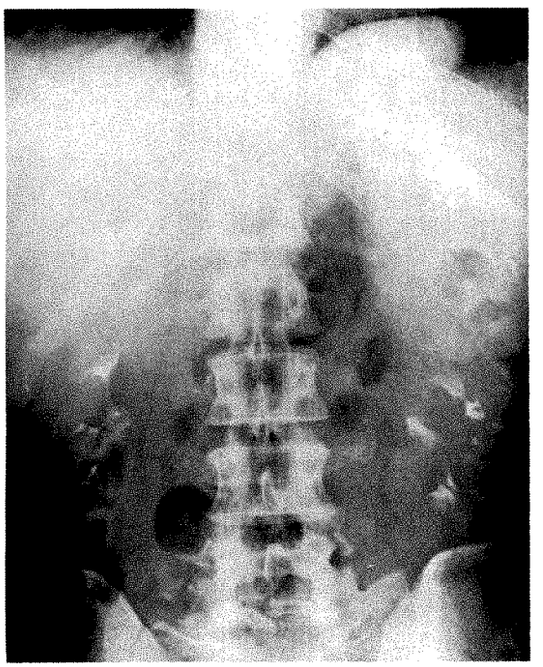


FIG. 1. Intravenous pyelogram. The spleen appears enlarged, and some irregular calcifications are demonstrated in the spleen.



FIG. 2. Selective celiac arteriogram. There is a stretching of the arteries surrounding the tumor. Marked displacement of the left kidney.

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FIG. 3. Selective celiac angiogram, capillary phase. An opacification of the remaining normal splenic tissue is seen only in the upper part of the spleen.

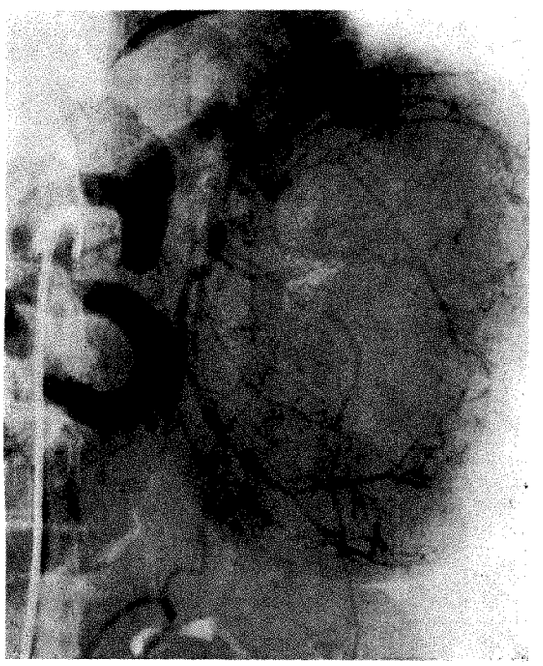


FIG. 4. Selective celiac arteriogram, subtraction film. The small, irregular "tumor vessels" are better visualized.

1). Several irregular calcifications were noted in the spleen.

Selective celiacography revealed a large mass occupying most of the spleen (Fig. 2; and 3). The lesion was considered to be a malignant tumor, and splenectomy was performed a few days later. The histologic examination of the specimen revealed a plasmocytoma. The postoperative course was uneventful, and during the following 6 weeks the sedimentation rate and serum protein values were normalized. The patient was free of symptoms at follow-up 3 years after the operation.[8]

DISCUSSION

Since Edsman[1] in 1954 reported a case of a malignant splenic tumor diagnosed by arteriography, several papers have been published on this matter.[1-4,6] The angiographic appearances of the present splenic mass were strongly suggestive of a malignant tumor. Some arteries were stretched and displaced circumferentially around the expansive lesion. The minor peripheral branches within the tumor had an irregular course with some caliber variation, and a corkscrew-like appearance (Fig. 4). The vascularization of the tumor was moderate. No "tumor blush" or abnormal arteriovenous shunting appeared. Most of the tumor was sharply outlined, except in the upper part where the border against the normal splenic tissue was more diffuse.

Hamartomas of the spleen are known to present a "malignant" arteriographic pattern.[3,4,9] However, calcifications in hamartomas are unusual.[3] Cyst walls often are calcified,[5] but the arteriographic pattern in the present case excludes this diagnosis.

Roentgen examination of the skeleton revealed no signs of destruction. The spleen was removed without difficulty. Most of it was occupied by a grapefruit-sized tumor with a thin capsule (Fig. 5). The total weight of the specimen was 1,030

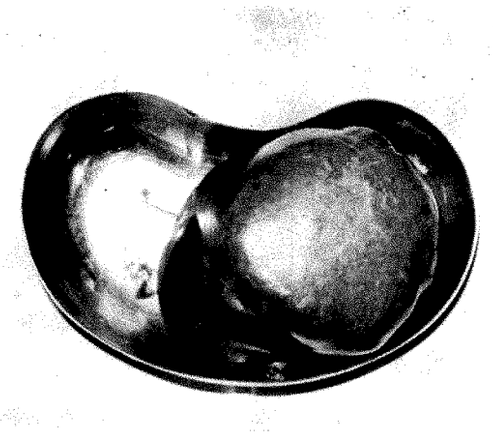


FIG. 5. Operative specimen, total weight 1,030 gm. Normal splenic tissue seen to the left, while the greater part of the spleen is occupied by the large tumor.

gm. The remaining splenic tissue in the upper part was microscopically normal. The tumor consisted mainly of plasma cells: some of them were binucleated, otherwise they were considered to be normal and only few mitoses were seen. The pathologists concluded on a definite diagnosis of plasmocytoma of the spleen.[7] The tumor was considered to be a primary lesion, and this was further supported by the abnormal values of serum proteins returning to normal shortly after removal of the tumor.

SUMMARY

A case of primary plasmocytoma of the spleen is reported.

The roentgenographic appearances of the tumor are presented.

The angiograms showed a vascular pattern within the tumor, that strongly suggested a diagnosis of a malignant tumor of the spleen.

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RADIATION THERAPY OF DESMOID TUMORS*

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THE desmoid tumor is an uncommon, benign neoplasm which arises from musculoaponeurotic structures. It is locally invasive but does not metastasize to lymph nodes or *via* the blood stream. This tumor in its extra-abdominal location was first defined and described by Nichols in 1923.[7] He emphasized the similarity between the extra-abdominal fibroma and the abdominal desmoid tumor. Recently, Stout and Raffaele[9] classified desmoid tumors under the general pathological heading of fibromatoses. This group includes fibromas, keloids, Peyronie's disease, plantar and palmar fibromatosis, fibromatosis colli, progressive myositis fibrosa, and desmoid tumors.

CLINICAL FEATURES

Most patients complain of a firm mass, usually fixed, which grows slowly and attains a large size before treatment is sought. Pain, if present, occurs as a late symptom. In 85 of a reported series of more than 650 cases of extra-abdominal fibromatosis, the shoulder girdle was the site of involvement.[9] In this location the brachial plexus may be affected, resulting in signs of motor weakness, numbness, or hypoesthesia. The tumor occurs in both sexes and may occur at any age, although it is most commonly seen in young adults.

PATHOGENESIS

Various theories of the pathogenesis of desmoid tumors have been advanced. Booher and Pack[2] have suggested that they are related to hormonal factors because of the frequent association of these tumors with pregnancy. They also postulated that a traumatic hematoma may form a nidus for the development of a desmoid tumor. The microscopic studies of desmoid tumors, however, have revealed no hemosiderin content. It was further postulated that this tumor could represent an autoimmune disease and that the aggregates of lymphoid tissues, sometimes noted at the margins of the tumor, could be involved in the autoimmune process.

PATHOLOGICAL FEATURES

The gross tumor is dense and hard. If the surface is cut the tumor bulges out and is white or pinkish in color. The interlacing bundles of white fibrous tissue are usually seen without difficulty and there is a remarkable tendency to invade surrounding structures. No capsule or definite line of cleavage exists between the tumor and adjacent muscle. The tumor may be attached to bone and cause erosion by pressure. Although the lesions have been found to surround vessels and nerves, to our knowledge invasion of these structures has not been reported—and no lymphatic or hematogenous metastases occur.

The histologic appearance consists of uniform, elongated, slender cells surrounded and separated from one another by abundant collagen. The cells do not have atypical, hyperchromatic, or bizarre nuclei. The nuclei are small, pale-staining, and sharply defined. The nucleoli are not prominent. Occasionally, mitotic figures may be present, but they are typical in configuration. The cells and collagen fibers are arranged in swirling or interlacing bundles or fascicles, which often merge with one another and form a dense, solid tumor mass. The fibrous tissue extends into and between muscle bundles for considerable distances, often isolating islands of muscle fibers.

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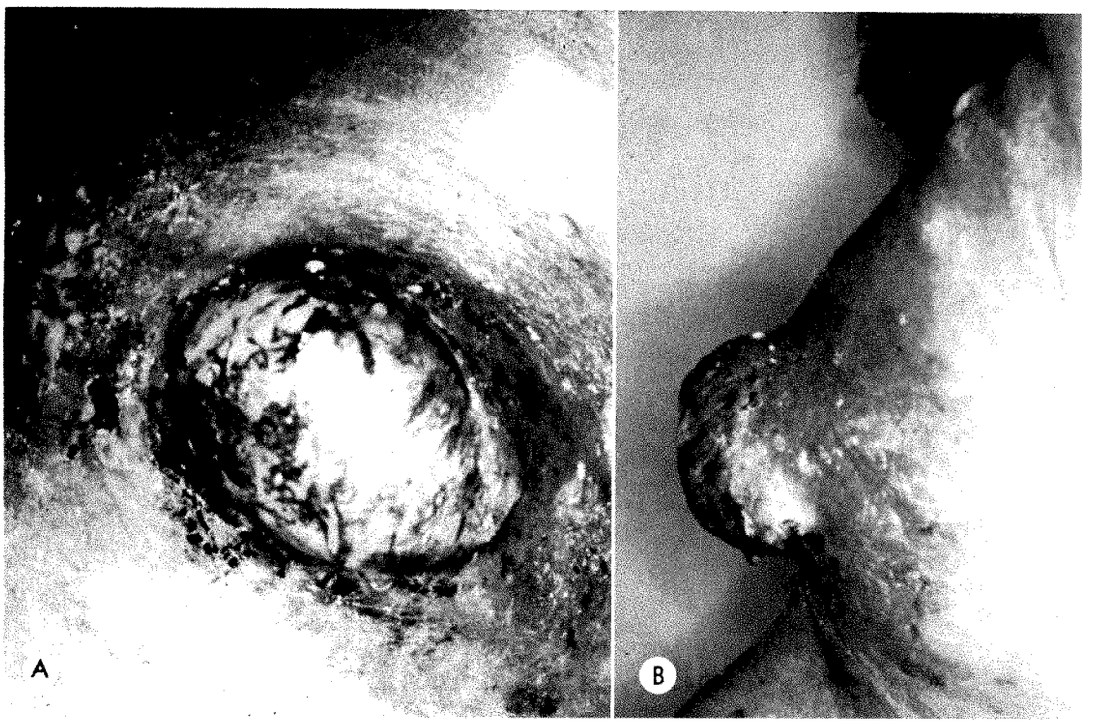


FIG. 1. Case 1. (*A*) Biopsy incision of soft tissue mass in right neck and shoulder, performed before radiation therapy. (*B*) Profile view showing herniation of tumor through the biopsy incision.

Distinction from a fibrosarcoma is readily apparent in the great majority of cases.

REPORT OF CASES

We have treated by means of definitive radiation therapy 4 patients with extensive desmoid tumors deemed unresectable by the referring or consulting surgeon.

CASE 1. A 69 year old woman from Samoa had a 1 year history of a slowly enlarging mass on the right side of her neck. At the time of examination it had attained a huge size. The mass extended from the lobe of the right ear laterally to the shoulder joint, anteriorly to the clavicle, and posteriorly into the trapezius muscle (Fig. 1, *A* and *B*). It was not tender but rock-hard. The patient could scarcely move her cervical spine because of the extent of the tumor. The radial pulse and arm sensation were normal, but there was some weakness in the right arm. Roentgenographic studies demonstrated the huge mass on the right side of the neck to be devoid of calcification (Fig. 2). A roentgenogram of the right shoulder showed an erosion on the medial surface of the scapula due to pres-

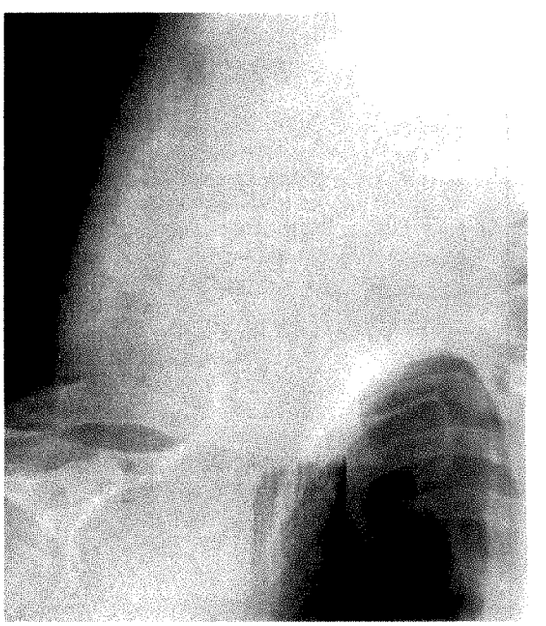


FIG. 2. Case 1. The large mass displaces the trachea and extends below the clavicle.

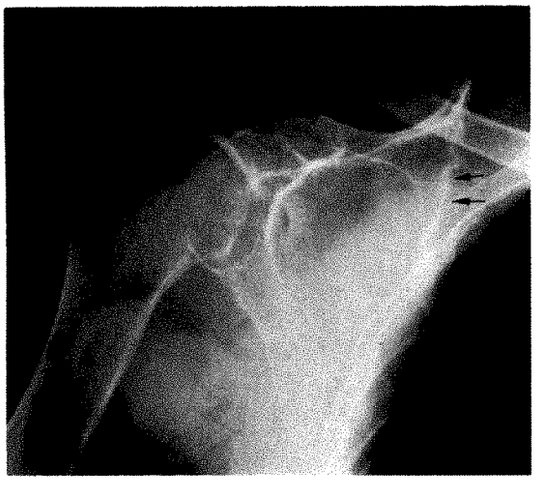


FIG. 3. Case I. Erosion defect (arrows) on medial border of the scapula caused by pressure of the tumor.

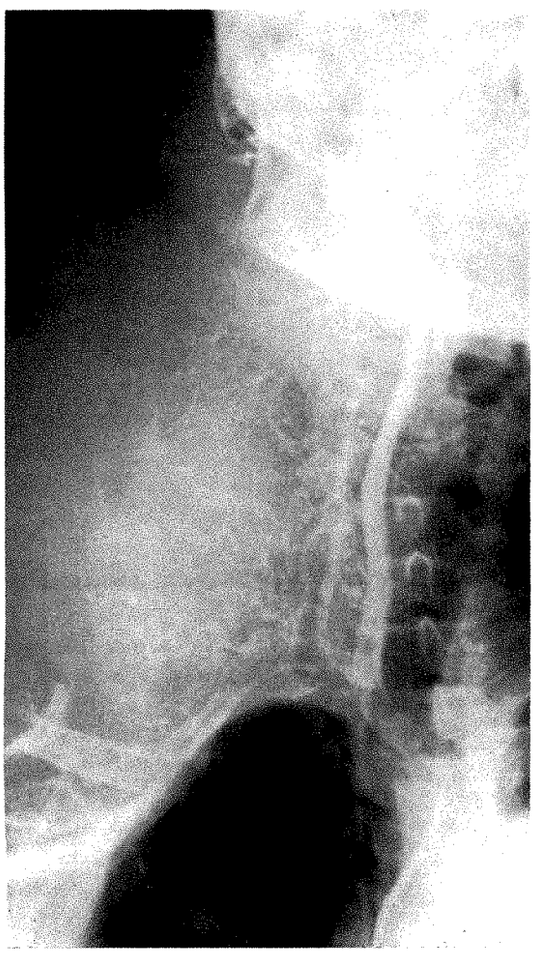


FIG. 4. Case I. Abnormal nonmalignant vessels seen within the tumor.

sure (Fig. 3). An axillary arteriogram was obtained which revealed abnormal nonmalignant tumor vessels within the large mass (Fig. 4). The tumor herniated through the biopsy incision. Biopsy revealed benign fibromatosis.

Definitive radiation therapy was undertaken with the use of a cobalt 60 teletherapy apparatus; the patient received 5,500 rads to the mid-plane of the mass, accomplished in 32 fractions over a 42 day period. On subsequent follow-up visits, there was seen slow resolution of the extensive mass with decrease in the amount of neck pain and increased range of motion of the cervical spine. At follow-up examination, 2 years after therapy, the patient was clinically free of disease (Fig. 5, *A* and *B*).

CASE II. A 32 year old Greek-American man had a radical resection of a large mass at the left shoulder girdle. The left clavicle, left anterior upper 3 ribs, and both pectoral muscles were removed *en bloc*. The pathologic diagnosis was desmoid tumor with thin surgical margins. One year later the tumor recurred. It was 8 cm. in diameter and fixed at the medial aspect of the surgical incision. The tumor had progressively enlarged. The recommendation by the Tumor Board was surgical exploration. It was found that the medial portion of the lesion adhered to the upper thoracic spine; the mass was therefore deemed unresectable. A biopsy was taken (Fig. 6).

The patient subsequently underwent therapy at the Section of Radiation Oncology. He had a hard lobulated axillary mass, measuring approximately 15 cm.×7.5 cm., which extended from the lateral border of the left scapula, across the axilla to the anterior axillary line. In addition there was a diffuse, hard, supraclavicular mass, measuring approximately 5 cm.×5 cm. The left arm was cold and dry, indicating involvement of sympathetic nerves; the radial pulse was absent. The patient was treated with definitive radiation therapy on a cobalt 60 teletherapy apparatus, receiving 6,100 rads to the mid-plane of the tumor, accomplished in 34 fractions over a period of 53 days. The following 2 year period has revealed slow resolution of the large mass and decrease in shoulder pain. The radial pulse is now present and there is no clinical evidence of disease.

CASE III. Rectal and vaginal examination of a 27 year old woman complaining of aching pain revealed a palpable mass. A laparotomy was

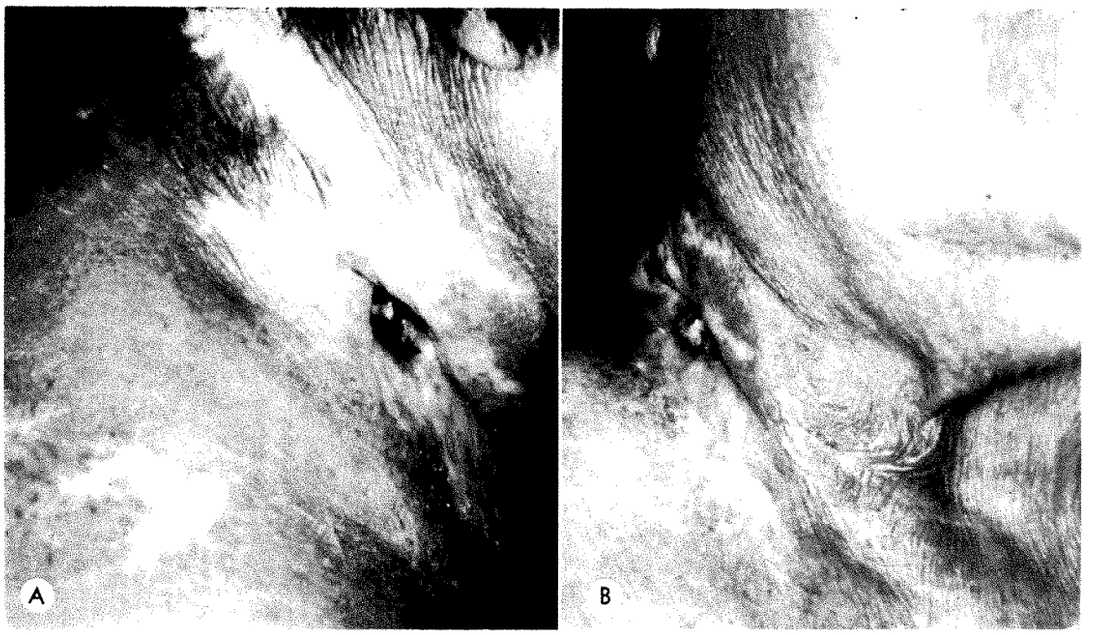


FIG. 5. Case I. (*A* and *B*) Marked resolution of the mass with a small persistent central ulcer.

undertaken in which a large presacral fibrous tumor was removed from the sacral hollow and left sacral plexus. The pathological diagnosis was that of a desmoid tumor. The patient did well until 2½ years later when examination showed a large mass on her left buttock. Further exploration revealed a 12 cm. × 10 cm. desmoid tumor, fixed to the surrounding structures in such a way that it could not be excised without sacrificing the sciatic nerve. The only surgical possibility would have been a hemipelvectomy and the surgeon postulated that even this procedure may not be successful because of the previous deep pelvic extension. The patient was subsequently referred for radiation therapy and was treated definitively on a 4 mev. linear accelerator, receiving to the mid-plane of the tumor a dose of 5,100 rads in 32 fractions over a 48 day period (Fig. 7). On subsequent follow-up visits there was gradual flattening of the left buttock, and the buttocks and thighs became almost symmetric (Fig. 8). At the present time, 2 years

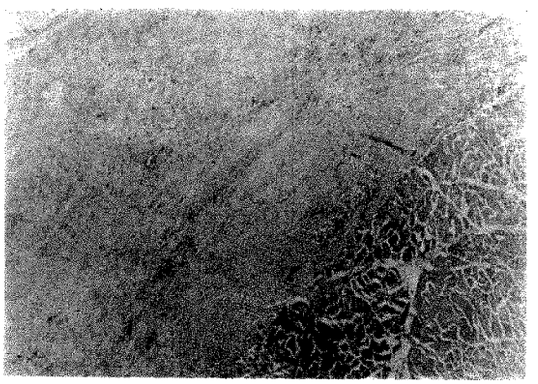


FIG. 6. Case II. Photomicrograph of biopsy specimen showing composition of tumor to be dense, relatively avascular, hypocellular bands of connective tissue (H and E stain; × 200). Adjacent skeletal muscle is seen to be surrounded in part by some of the fascicles of connective tissue.



FIG. 7. Case III. Mass on left buttock near completion of radiation treatment. Note distortion of contour and radiation pigmentation.

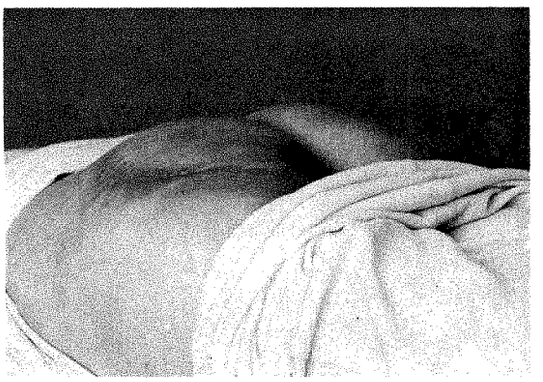


FIG. 8. Case III. Two years after treatment. The left buttock shows nearly normal contour.

after therapy, the patient gives no clinical evidence of recurrent disease.

CASE IV. A 22 year old man had a 4 month history of a slowly enlarging mass on the lower right portion of his neck, which was painful (Fig. 9). Biopsy was performed revealing fibromatosis (Fig. 10). Surgical exploration was subsequently carried out which exposed a large, firm, pale, tumor mass that occupied the base of the neck on the right and extended under the right clavicle to the midline and the trapezius posteriorly. The mass appeared to fuse with the prevertebral fascia and merge laterally with the roots of the brachial plexus. The surgeon feared injury to the brachial plexus and therefore did not proceed with any aggressive surgical resection. The patient was referred to us and treated on the 4 mev. linear accelerator with a mean tumor dose of 5,500 rads in 30 fractions over a 43 day period. Follow-up visits have shown

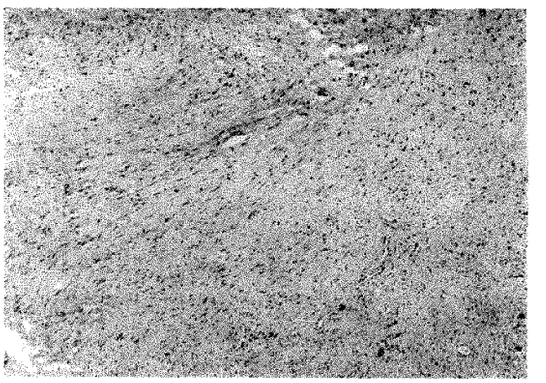


FIG. 10. Case IV. Section of tumor showing proliferation of well differentiated fibroblasts growing in interlacing bundles (H and E stain; ×200). The nuclei are very thin, flattened and pyknotic.

progressive resolution of the extensive tumor. At the last patient visit, 12 months after completion of therapy, the tumor had regressed to 20 per cent of its original size (Fig. 11).

DISCUSSION

Desmoid tumors present a difficult problem in evaluation and management because of the discrepancy between their apparently harmless microscopic appearance and their potential to attain a large size, to recur, and to infiltrate adjacent structures in a manner suggestive of fibrosarcoma. The recurrence rate following surgical excision is high, 17 of 30 (57 per cent) reported by Enzinger and Shiraki,[4] 5 of 18 (27 per cent) reported by Pack and Ehrlich,[8] and 10 of 29 (35 per cent) reported by Hunt



FIG. 9. Case IV. Frontal view of large mass at right base of neck before treatment by irradiation.

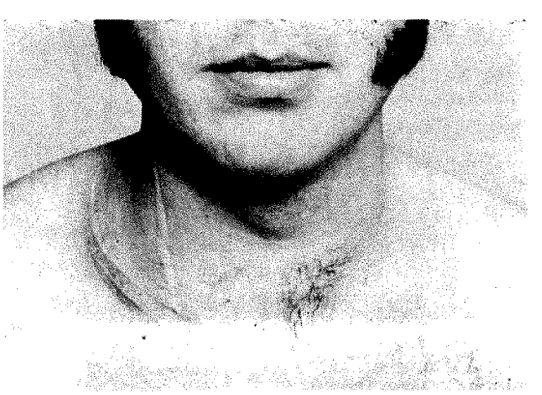


FIG. 11. Case IV. Twelve months after radiation therapy. The tumor has regressed considerably.

et al.[5] This high recurrence rate had led surgeons to adopt more radical approaches in an attempt to control this benign but locally aggressive lesion. Das Gupta and associates[3] feel that major amputation is the treatment of choice in recurrent large tumors of the iliac fossa, gluteal fold, or shoulder. Experience with irradiation in the treatment of desmoid tumor is limited. Musgrove and McDonald[6] were not convinced of the value of radiation, but 5 of 7 patients who had radiation therapy in their series of 35 showed no recurrence. Hunt *et al.*[5] feel that radiation plays no part in the management of desmoid tumors; they admit, however, to no personal experience. Pack and Ehrlich[8] indicate radiation therapy to be useful in inoperable tumors (3 of 3 patients were free of recurrence at 5 years) and in recurrent tumor following surgery (3 of 4 patients showed good results). Benninghoff and Robbins[1] advise radiation therapy for inoperable, incompletely removed, and recurrent tumors.

Radical, mutilating surgery for this relatively benign lesion should be seriously questioned. In our modest series, 3 patients with extensive, unresectable tumor, have been free of disease for more than 2 years after radiation therapy. Presently, the fourth patient has shown considerable regression of a huge tumor, just 12 months after therapy. The tumors usually recur during the first months after radiation treatment,[4] but the first few months constitute too short a follow-up period to predict ultimate control. As a last resort, radical surgery (such as forequarter or hindquarter amputation) could be performed if properly administered therapy with modern megavoltage equipment has been unsuccessful.

SUMMARY

Four patients with extensive, unresectable desmoid tumors were treated with definitive radiation therapy.

Three are free of disease 2 years after treatment; the tumor of the fourth has decreased to 20 per cent its former size 1 year after therapy by irradiation.

The authors feel that surgery is the treatment of choice in cases of small lesions, but radiation therapy should be attempted in the more extensive tumors. Radical amputation should be reserved for only those patients in whom desmoid tumors failed to respond to radiation treatment.

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XEROMAMMOGRAPHY—AN IMPROVED DIAGNOSTIC METHOD*

A REVIEW OF 250 BIOPSIED CASES

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XERORADIOGRAPHY has excited the attention of radiologists since 1955, when Roach published his first work on xeroradiography of bones. The xeroradiographic work of Ruzicka *et al.*[8] in mammography in 1965 seemed promising and attracted the attention of Wolfe,[9] who obtained one of the xeroradiographic units and did extensive work in xeromammography.

Through the interests of the American College of Radiology Committee on Breast Disease and an *Ad Hoc* Committee of the American Cancer Society, the value of xeroradiography has been extensively investigated. The author was fortunate to have the privilege of working with one of the experimental xeroradiographic units.

Low kv. tungsten techniques were used. Low kv. readings vary from one roentgenographic unit to another. In this series 30–40 kv. was employed at 300 mas. to 450 mas., depending on the desired contrast. Xerographic charging factors were 1,600 V_0, 8 bursts of powder, and positive imaging. The breasts were compressed by a compression device.

The initial intent of this study was to do conventional Egan technique mammograms and xeromammograms on all patients until 250 patients had been biopsied. It became evident after a double study was done on 100 patients that it was unnecessary to continue the conventional film mammogram studies. Because of the high resolution and wide latitude of the xeroradiographic process, there was considerably more information on the xeromammograms than on the conventional film mammograms. The increased information of the xerograms necessitated a relearning process in the interpretation of the mammograms. Of particular importance was the fact that some carcinomas could not be diagnosed on the conventional film mammograms, but were clearly evident on the xeromammograms. Early in the comparative study 2 carcinomas in dense breasts could not be seen of the conventional film mammograms, but were readily identified on the xeromammograms. Of further importance was the ease of reading the xeromammograms without fatigue in relation to the labor required in evaluating conventional studies: 3 to 5 minutes are needed to read the conventional film mammograms, with less confidence than a xerogram which can usually be read in less than 1 minute.

We have found the xeromammographic process to be reproducible and of significant importance in increasing diagnostic accuracy in diagnosis of breast disease, as reflected in our first 250 breast biopsies.

MATERIAL AND METHOD

In order to obtain 250 biopsies we examined 1,535 patients by the xeroradiographic technique and ended up with the sum total of 277 biopsies. In this group of biopsies, there were 54 carcinomas; there was 1 overcall (Fig. 1, *A* and *B*) and 3 undercalls; the other 223 were of benign disease.

In reporting xeromammograms a direct method of reporting was used, an attempt being made to give a histologic diagnosis if possible. A summary of the reports is given in Table 1.

Thirty-nine patients were reported as having carcinoma, 38 of these were carcinomas; 10 were reported as suspicious

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of carcinoma and all of these were carcinomas. There was a group of 20 cases in which there was an atypical area within the breast, which is best described as an area of asymmetry of breast tissue when compared to the opposite breast (Fig. 2, *A* and *B*), or an area of what appeared to be unusual duct activity in relation to the rest of the breast tissue in that particular breast. Of this group of 20 reported as atypical areas and biopsy indicated, 2 were carcinomas and 18 were benign lesions. It is of interest that in these 18 the histologic reports were all of active hyperplasia of duct systems, with several being reported as showing areas of atypia.

There was another group of 10 cases, in which there were dilated isolated subareolar ducts. Biopsy is thought to be indicated where a solitary dilated subareolar duct is noted, as this may be an indirect sign of carcinoma. Frequently, these ducts will contain some form of intracellular debris (Fig. 3*A*); infrequently, they will contain intraductal papilloma (Fig. 3*B*); and more rarely they will contain carcinomas (Fig. 3*C*). In the group of 10 cases in which biopsy was urged in this series, 1 had a noninvasive intraductal carcinoma. When multiple dilated ducts are seen, the examiner assumes that these are on an inflammatory basis and merely reports them as such.

TABLE I

METHOD OF REPORTING

Xeromammographic Diagnosis	Pathology Diagnosis	
	Carcinoma	Benign
Carcinoma	38	1
Suspicious of Carcinoma	10	0
Atypical Area,* Biopsy Indicated	2	18
Dilated Isolated Subareolar Duct, Biopsy Indicated	1	9
Localized Cluster of Calcification, Biopsy Indicated†	0	–
Benign Disease	3	188
Total—277	54	223

* Asymmetry of breast tissue in opposite breasts.
† Clusters of sclerosing adenosis type.

There was also a series of 7 cases with localized clusters of isolated calcification without a mass, in which biopsy was recommended. It should be pointed out that a number of the carcinomas had what was thought to be diagnostic calcifications present and are not included in this category. This is the group of clustered calcifications that are usually associated with sclerosing adenosis (Fig. 4), and are sometimes indirect evidence of an adjacent

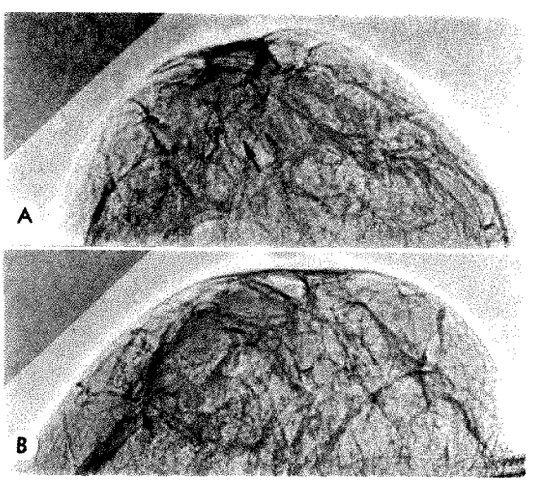


FIG. 1. (*A* and *B*) Overcall: xerographic report, comedo carcinoma; pathology report, sclerosing adenosis.

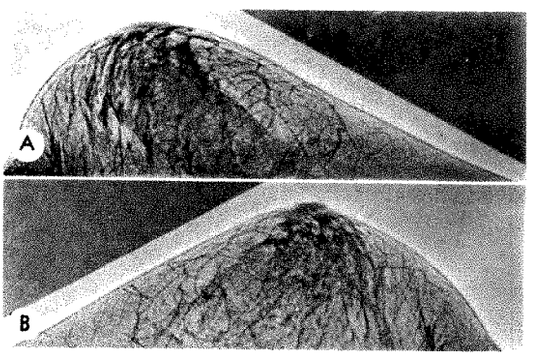


FIG. 2. A 37 year old female with a clinically questionable mass in the right breast. (*A*) The image of the right breast when compared with (*B*) the image of the left breast shows a gross asymmetry of breast tissue, there being a considerably greater density within the centrum of the right breast than the left breast. This asymmetry or atypical area is frequently a diagnostic sign of carcinoma.

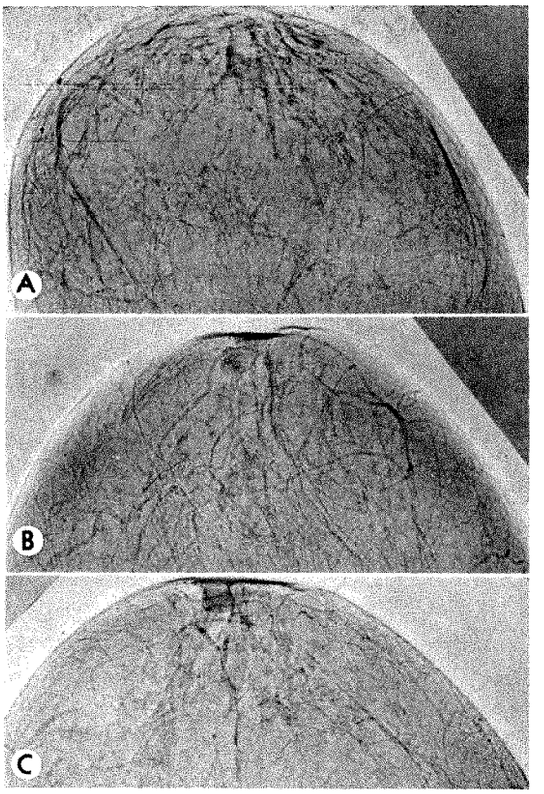


FIG. 3. (*A*) Isolated dilated subareolar duct containing intracellular debris and old hemorrhage. (*B*) Isolated dilated subareolar duct containing intraductal papilloma. (*C*) Isolated dilated subareolar duct containing noninvasive intraductal carcinoma.

area of lobular carcinoma *in situ*. These 7 cases all had benign sclerosing adenosis, none of which was identified as malignant histologically. Many more calcifications are seen in xeromammography than in conventional mammographic studies.

In the remaining group of 191 cases of

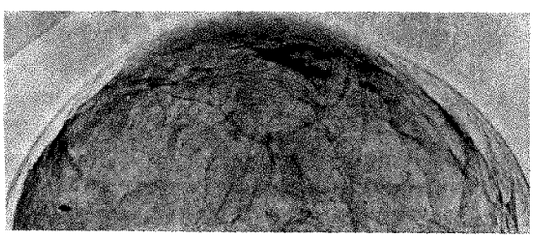


FIG. 4. Dense glandular breast in a 26 year old female with localized collection of punctate calcifications of the sclerosing adenosis type (arrow).

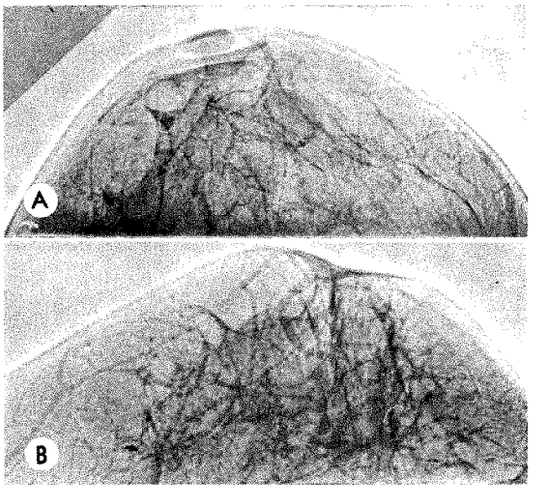


FIG. 5. (*A* and *B*) Undercall: 45 year old female; xerographic report, mass in the upper inner quadrant presumed to be cystic; pathology report, scirrhous carcinoma. (In review of the xerograms an arrow is placed on what probably represents the carcinoma.)

radiologically reported benign disease, 3 had carcinomas, and the other 188 cases had benign disease as reported; thus, 3 carcinomas were missed. In 1 case the carcinoma was only questionably imaged (Fig. 5, *A* and *B*). In retrospect, the second case should have been recognized (Fig. 6, *A* and *B*). The third case was in a premenopausal female with a rapidly growing neoplasm (Fig. 7, *A* and *B*).

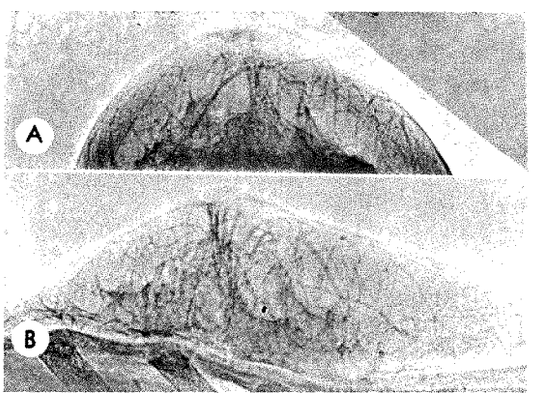


FIG. 6. (*A* and *B*) Undercall: xerographic report, an atypical area of breast tissue in an asymmetric position presumed to be fibrocystic disease; pathology report, invasive duct carcinoma.

DISCUSSION

The most important facet of this study was the number of occult carcinomas: 13 of the carcinomas were clinically occult. In establishing these as clinically occult, the referring physician was always given the benefit of the doubt when there was a question of a palpable mass. These 13 patients were referred for: examination of the opposite breast; routine mammography, based on the findings of a yearly check-up with Papanicolaou smear; follow-up serial study in women of high risk groups and of women with previous mastectomies. A point of significant importance is the fact that 11 of the patients with clinically occult carcinomas had negative axillary lymph nodes, 1 case with comedo carcinoma had 1 involved axillary lymph node, and the other case presented with metastatic bone disease and clinically negative breasts.

Clinically occult carcinomas may appear obvious radiologically. A good example of this is the comedo carcinoma, primarily an intraductal carcinoma, which may measure radiologically 3 to 4 cm. in diameter and still be noninvasive or minimally invasive (Fig. 8, *A* and *B*). For this reason, large lesions of this type are frequently clinically negative. This type of

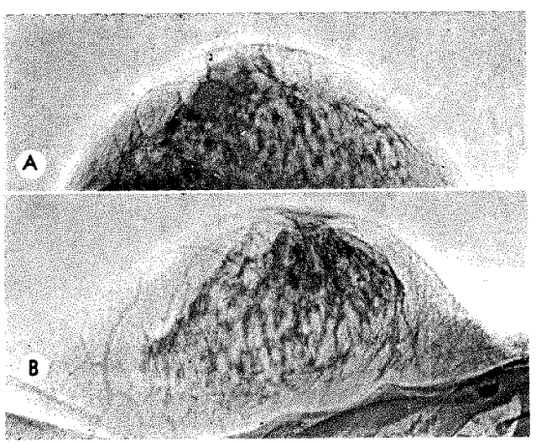


Fig. 7. (*A* and *B*) A 47 year old female; xerographic report, mass in the subareolar area of upper outer quadrant presumed to be fibrocystic disease; pathology report, highly invasive undifferentiated carcinoma.

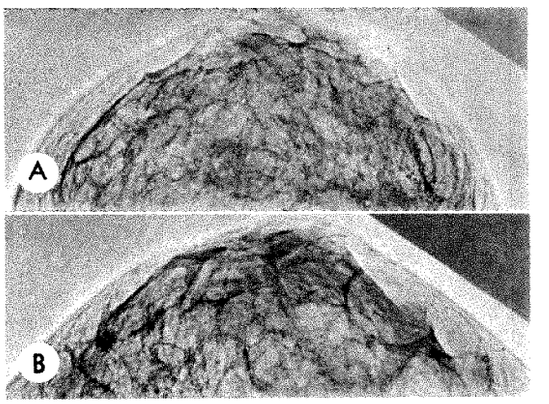


Fig. 8. (*A* and *B*) Comedo carcinoma.

case is of major importance in understanding carcinomas to both the radiologist and the surgeon. The radiologist primarily diagnoses by recognition of an image pattern which is produced by an invasive mass as, for example, the stellate[3] or scirrhous carcinoma. This invasive mass is the clinically presenting dominant lesion. As long as the carcinoma is intraductal or minimally invasive, most of the radiological signs are indirect. The comedo carcinoma is an example of this, being radiologically identified by typical intraductal calcifications without an associated mass. Thus, the surgeon does not feel this lesion until the invasion is somewhat more extensive.

A more subtle indistinct sign of carcinoma is the dilated isolated subareolar duct as discussed above. Areas of atypical duct disease, as described by Gallagher and Martin[5] may be an early sign of carcinoma. In these cases the radiologist does not actually see the carcinoma, but a reactive type of periductal collagenosis which has apparently been excited by the carcinoma. This same type of collagen excitation is observed in the developing carcinoma.[6] The 2 carcinomas, one found in serial breast studies where a new density occurred in the breast tissue, and the other an intraductal or minimally invasive lesion, were among the 13 clinically occult carcinomas.

Mammograms are routinely obtained, as follow-up on 6 to 12 months basis, on pa-

TABLE II

AGE DISTRIBUTION

Age Groups (yr.)	No. of Patients
20	1
30	4
40	8
50	23
60	10
70	8

tients with previous mastectomies. Seven of our 54 carcinoma patients had previous mastectomies and 4 of these were in the clinically occult group. Gallagher and Martin,[3] in their study of correlation of mammograms with whole organ section of the breast, have found carcinoma to be of multicentric origin with a high incidence of bilateral breast carcinoma. It seems possible that many women now dying from carcinoma of the breast may be dying from metastasis from an unsuspected primary carcinoma of the opposite breast.

In analyzing the age range (Table II) of the patients with carcinomas in our group, the youngest patient was 25 years of age and represented the only patient in the twenties. There were 4 carcinomas in the 30 year age group; 8 in the 40 year age group; 23 in the 50 year age group; 10 in the 60 year age group; and 8 in the 70 year age group, the oldest patient being 79 years old. Fifty of the patients were married or had been married and 4 were single. There was a family history of breast cancer in 6 patients; 40 of these patients were menopausal, and 14 were premenopausal. As previously mentioned, 7 of the patients had had previous mastectomies which represented 7.7 per cent of the cancers in our series.

Thirty-four of the 54 carcinoma patients sought attention because of a mass in a breast found on self examination; 7 were found by surgeons on a routine examination. The other 13 were unsuspected carcinoma cases. Twenty of the carcinomas were in the right breast and 34 were in the left breast. Of the 13 cases of occult carcinomas, there were 4 patients aged 38, 39, 41 and 46 years, who were premenopausal. The others had hysterectomies or were normally menopausal. Forty-one presented with a mass and 13 without a mass. The masses were either knobby (Fig. 9, *A* and *B*), stellate (Fig. 10, *A* and *B*) or mucinous types (Fig. 11, *A* and *B*), which have recognizable radiographic characteristics; 13 of the carcinomas exhibited calcium in some form; 2 had linear intraductal calcifications—a diagnostic sign. The size of the carcinomas, where masses were present

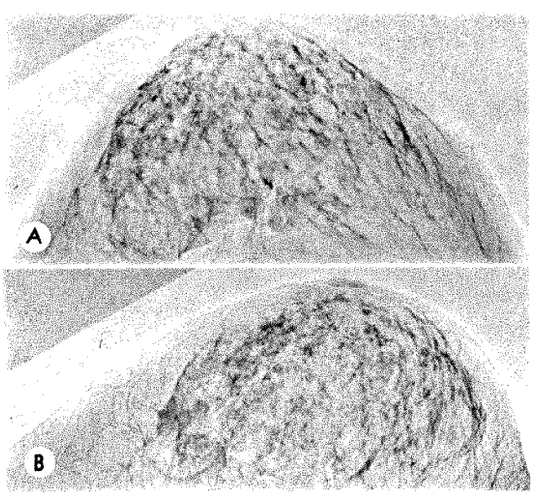


FIG. 9. (*A* and *B*) Classic knobby carcinoma.

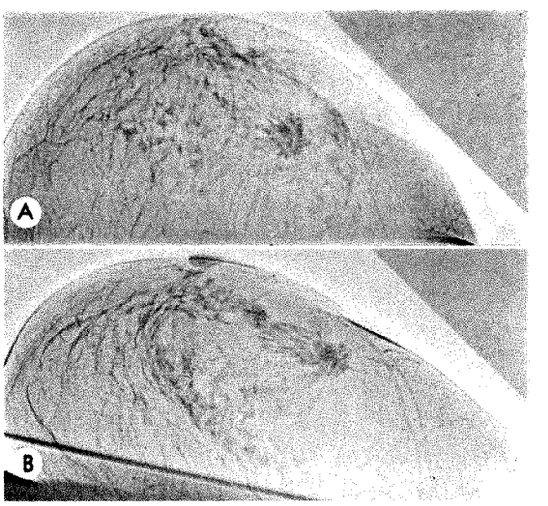


FIG. 10. (*A* and *B*) Classic stellate carcinoma.

in this series, varied from 3 mm. to 5½ cm. (Table III).

In 1 case there were 3 separate carcinomas by xeroradiography, measuring 2, 1½, and 1 cm., respectively. The remainder of the lesions had no masses and were diagnosed by indirect signs. Four had coarse intraductal calcifications, the comedo carcinomas. Only 2 carcinomas had clusters of fine calcifications. The other 5 had calcifications associated with areas of tumor necrosis.

Presumably because of the many small malignancies, 33 patients had negative axillary lymph nodes, 17 had positive lymph nodes, 3 had no lymph node resections, and only 1 had bone metastasis.

If cure rates in carcinoma are to improve significantly, improved methods of diagnosis of breast disease must be diligently sought. Xeromammography certainly appears to offer a better modality for finding these carcinomas than the conventional film mammographic studies. By the same token, with the ease of reading and recognition patterns in xeromammography, a better understanding of benign disease of the breast should become evident.

In the benign cases in this series, the type of benign disease was recognized by radiologic patterns in most of the cases and confirmed histologically. Fibrocystic disease, adenosis, sclerosing adenosis, cysts (Fig. 12), adenomas and benign calcifications are easily identified once the recognition patterns are learned.

TABLE III

SIZE OF CARCINOMAS

No. of Carcinomas	Size
3	3 mm.
2	5 mm.
3	7 mm.
1	8 mm.
1	9 mm.
16	1–1.5 cm.
9	2–2.5 cm.
4	3–3.5 cm.
1	4.5 cm.
1	5.5 cm.

CONCLUSION

Xeromammography appears to be a superior method of diagnosing carcinomas of the breast.

Despite the handicap of working with an experimental xeroradiographic unit, and of a relearning process in diagnostic pattern recognition, 13 clinically occult carcinomas were found in a limited series of 250 biopsied cases.

The ease of reading images is time saving and the over-all diagnostic accuracy is superior to other methods.

At this time the only apparent chance for increased survival in breast cancers is in earlier diagnosis, and xeromammography seems to offer this opportunity.

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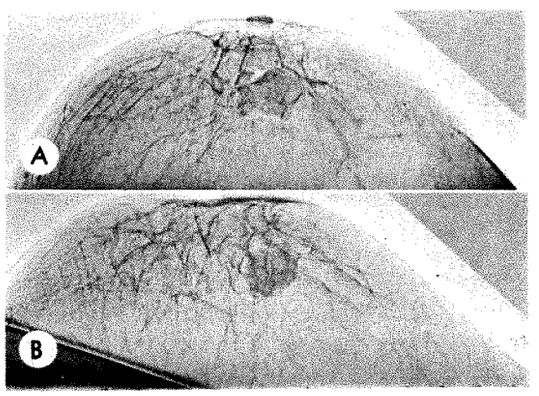


FIG. 11. (*A* and *B*) Medullary carcinoma, identified by a sharply marginated mass with a dilated duct radiating to the subareolar area.

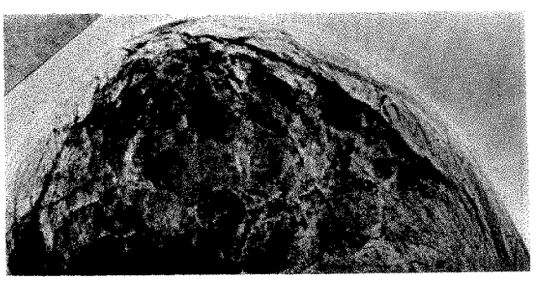


FIG. 12. Multiple cysts.

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HYPERNEPHROMAS WITH MASSIVE ARTERIOVENOUS FISTULAS*

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DESPITE the increased frequency with which this lesion has been reported within the past 10 years, hypernephroma with massive arteriovenous fistula remains an uncommonly encountered entity. Wise *et al.*[12] reviewed the literature in 1967 and found 7 cases, to which they added 3 of their own. Elkin[5] in 1971, reviewing renal arteriovenous fistulas in general, added 5 cases which were associated with renal cell carcinoma. The emphasis in the literature has been on the cardiovascular manifestations associated with this entity, with their prompt relief following removal of the tumor. Elkin,[5] however, in reporting his 5 cases found no cardiovascular symptoms or findings which could be directly attributed to the arteriovenous fistula.

The purpose of this communication is to report our experience and findings in 4 cases of hypernephroma with massive arteriovenous fistula encountered within the past 2 years at our institutions.

REPORT OF CASES

CASE I. M.B., a 67 year old white female, was admitted for evaluation of a 50 lb. weight loss occurring over the past 2 years. Past history disclosed one episode of congestive heart failure 2 years previously. Physical examination upon admission revealed a blood pressure of 140/60 mm. Hg in both upper extremities. The heart was enlarged, and there was a Grade 4–6 pansystolic murmur heard over the entire precordium. The liver edge was palpable 8 cm. below the right costal margin. No abdominal masses or bruits were detected. There was 2+ pitting edema of both lower extremities. Admission laboratory data revealed a Hg of 10.0 gm. per cent and a hematocrit of 30 per cent. Urinalysis was normal. A chest roentgenogram showed cardiomegaly; in addition, there were nodular lesions throughout both lungs thought to be metastases. A search for a tumor was begun, and an intravenous pyelogram revealed a mass lesion in the medial aspect of the superior pole of the right kidney (Fig. 1*A*). Aortography and selective right renal arteriography showed a mass lesion in the upper pole of the right kidney with typical pathologic vessels characteristic of hypernephroma (Fig. 1*B*). The right renal artery was slightly enlarged and there was opacification of the inferior vena cava, while contrast material was still seen in the renal artery, indicating a massive arteriovenous fistula. Due to the metastases to the chest and the patient's borderline cardiovascular status, it was elected not to perform surgery. She was treated with chemotherapy and discharged and has not had follow-up at our hospital.

CASE II. E.B., a 45 year old white male, was admitted for the evaluation of hematuria. One year prior to admission the patient noticed 1 episode of hematuria. He was asymptomatic until 3 weeks prior to admission when he noticed 6 episodes of intermittent hematuria. He saw a physician at this time, and his blood pressure was noted to be 210/130 mm. Hg. He had no prior history of hypertension, renal or cardiac disease. Physical examination upon admission was normal except for blood pressure of 210/140 mm. Hg recorded in both arms. No abdominal masses were palpable and no bruits were heard over the abdomen. Admission laboratory data revealed a Hg of 16.9 gm. per cent and a hematocrit of 47.5 per cent. Urinalysis showed no evidence of hematuria. An intravenous pyelogram demonstrated a mass lesion, 5 cm. in diameter, occupying the lower pole of the right kidney (Fig. 2*A*). Notching of the right ureter was also noted. Aortography revealed a highly vascular mass occupying the lower pole and hilum of the right kidney (Fig. 2*B*). Tumor vessels were seen in the lower portion of the mass. Opacification of the inferior vena cava was seen 1 second following visualization of the

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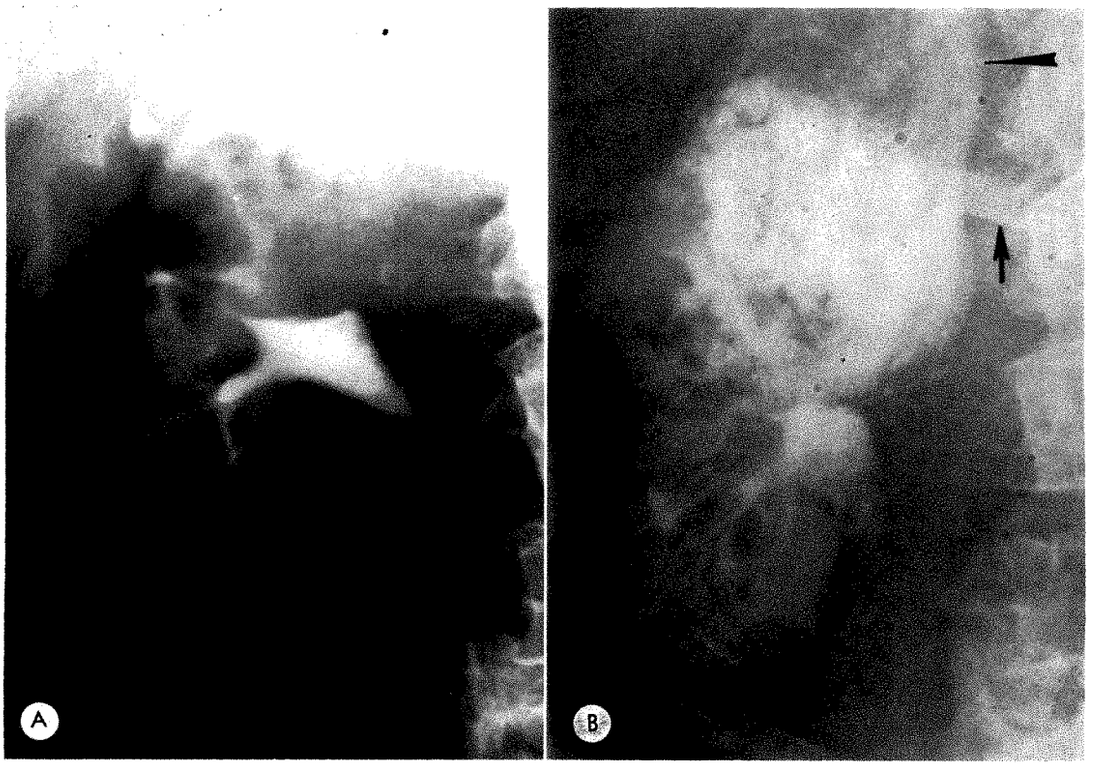


FIG. 1. Case I. M.B., a 67 year old white female.

(*A*) Intravenous pyelogram demonstrates a mass lesion in the medial aspect of the superior pole of the right kidney with distortion of the upper pole calyces and renal pelvis. (*B*) Selective injection of the right renal artery reveals a highly vascular tumor mass in the upper pole, with pathologic vessels characteristic of hypernephroma. The right renal artery (arrow) is slightly enlarged and there is opacification of the inferior vena cava (arrowhead) while there is still contrast material in the renal artery, indicating that a massive arteriovenous fistula is present.

artery, indicating a massive arteriovenous fistula (Fig. 2*C*). At surgery, a large arteriovenous fistula with palpable thrill was first encountered. The renal artery and vein were enlarged to 3 times their normal size. After ligation of the renal artery, a 3.5 × 5 cm. tumor mass was present in the lower pole of the right kidney. The renal vein had been invaded by the tumor mass. A right adrenalectomy and nephrectomy were performed. The pathologic diagnosis was hypernephroma with arteriovenous fistula and invasion of the main renal vein by tumor. The patient's postoperative course was uneventful. His blood pressure returned to normal (130/80 mm. Hg, both arms) within 10 days following surgery and has remained so on 2 subsequent follow-up visits.

CASE III. S.G., a 76 year old white female, presented with a history of 1 episode of hematuria and excruciating right flank pain 3 weeks prior to admission. Physical examination on admission showed a blood pressure of 160/70 mm. Hg in both upper extremities. Heart and lungs were within normal limits. No abdominal masses were palpable and no bruits were heard. Admission laboratory data revealed a Hg of 13.0 gm. per cent and a hematocrit of 37 per cent. Urinalysis was negative for red blood cells. Chest roentgenograms showed slight cardiomegaly. Cystoscopy was normal. An intravenous pyelogram demonstrated a mass lesion in the superior pole of the right kidney and notching of the right ureter (Fig. 3*A*). A flush aortogram demonstrated a highly vascular mass lesion in the upper pole of the right kidney with typical neovascularity of hypernephroma (Fig. 3*B*). There was simultaneous visualization of the right renal artery and inferior vena cava, indicating a massive arteriovenous fistula

(Fig. 3*B*). Dilated, tortuous periureteral arteries accounted for the ureteral notching on the right side. The patient refused surgery and no further diagnostic work-up was performed. She was discharged to be followed as an outpatient.

Case IV. R.B., a 68 year old white male, was admitted for evaluation of painless hematuria of 1 day's duration. His past history was negative for serious illness or trauma. Physical examination upon admission showed a blood pressure of 160/85 mm. Hg in both upper extremities. The heart and lungs were normal. There was a large mass palpable in the left upper quadrant which was movable and nontender. No abdominal bruit was audible. Admission laboratory data revealed a Hg of 12.7 gm. per cent and a hematocrit of 36.9 per cent. Urine specimen was loaded with red blood cells. Chest roentgenograms were within normal limits. Cystoscopy revealed blood coming from the left ureteral orifice. Intravenous pyelogram with tomograms demonstrated a huge mass occupying the lower pole of the left kidney, obliterating the lower pole calyces (Fig. 4*A*). Blood clots

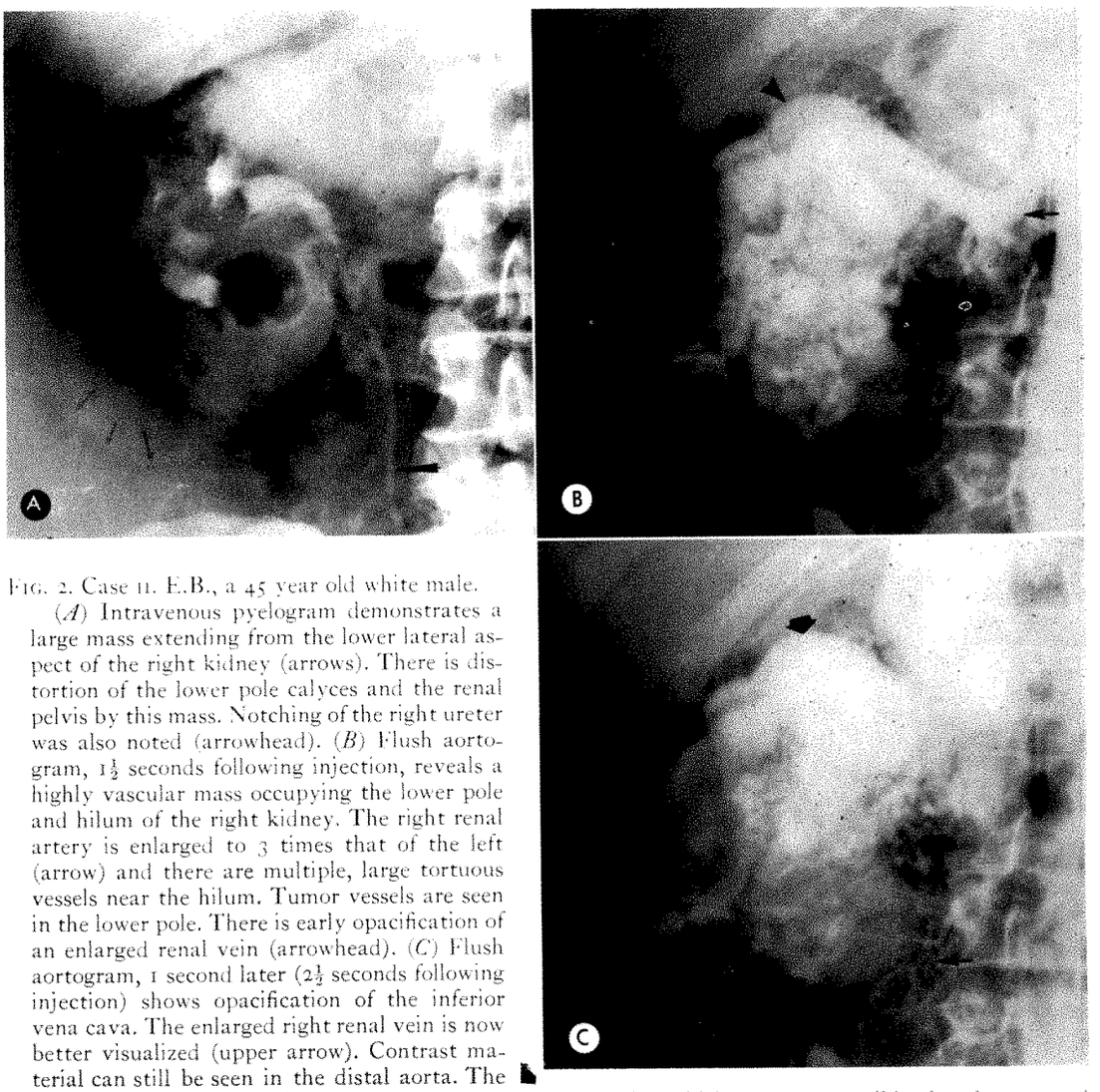


Fig. 2. Case II. E.B., a 45 year old white male.
(*A*) Intravenous pyelogram demonstrates a large mass extending from the lower lateral aspect of the right kidney (arrows). There is distortion of the lower pole calyces and the renal pelvis by this mass. Notching of the right ureter was also noted (arrowhead). (*B*) Flush aortogram, 1½ seconds following injection, reveals a highly vascular mass occupying the lower pole and hilum of the right kidney. The right renal artery is enlarged to 3 times that of the left (arrow) and there are multiple, large tortuous vessels near the hilum. Tumor vessels are seen in the lower pole. There is early opacification of an enlarged renal vein (arrowhead). (*C*) Flush aortogram, 1 second later (2½ seconds following injection) shows opacification of the inferior vena cava. The enlarged right renal vein is now better visualized (upper arrow). Contrast material can still be seen in the distal aorta. The lower arrow points to dilated tortuous periureteral arteries which were responsible for the ureteral notching.

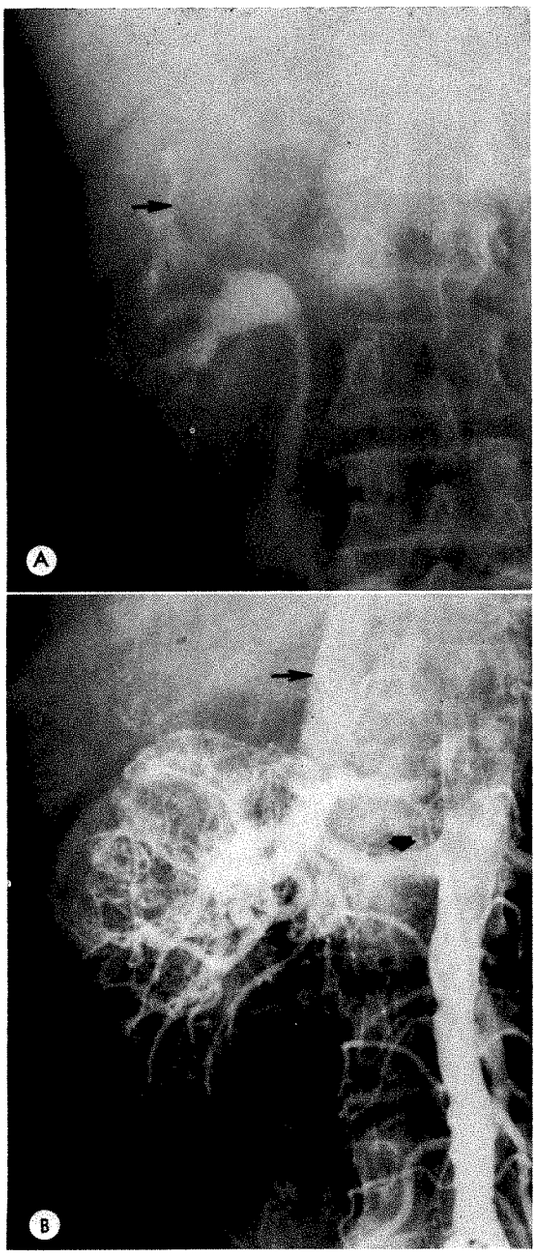


FIG. 3. Case III. S.G., a 76 year old white female.

(*A*) Intravenous pyelogram demonstrates a mass in the upper medial aspect of the right kidney with distortion of the upper pole calyces (upper arrow). There is notching of the right proximal ureter (lower arrow). (*B*) Flush aortogram demonstrates a highly vascular mass with tumor vessels occupying the superior pole of the right kidney. There is simultaneous visualization of the renal artery (broad arrow) and inferior vena cava (upper arrow). A network of dilated periureteral arteries (arrowhead) was noted and was responsible for the ureteral notching.

were noted in the left renal pelvis. Aortography and selective left renal arteriography demonstrated a 12 cm. in diameter mass in the lower pole of the left kidney (Fig. 4*B*). Tumor vessels were present in the upper portion of the mass. The lower portion was avascular and felt to represent cystic degeneration within the hypernephroma. The left renal artery was enlarged and an arteriovenous fistula was demonstrated with early filling of the left renal vein and inferior vena cava (Fig. 4*C*). At surgery, a large tumor was encountered in the lower pole of the left kidney. The left renal artery and vein were enlarged and a palpable thrill was present over the renal hilus. The pathologic diagnosis was hypernephroma with invasion of the large vessels about the renal hilus. There was cystic degeneration noted in the lower aspect of the tumor. The patient's postoperative course was uneventful.

DISCUSSION

CLINICAL FEATURES

Cardiovascular symptoms and findings were a prominent feature in only 1 of our cases (Case II). This 45 year old white male, who had no antecedent history of high blood pressure, was noted to have marked diastolic hypertension on admission. There was prompt return of his blood pressure to normal following nephrectomy. Roentgenographically, his was the most massive of the arteriovenous fistulas in our series. Another patient (Case I) did have cardiomegaly, a systolic murmur, and evidence of cardiac decompensation on admission. She did not have diastolic hypertension. It is difficult to directly relate this patient's symptoms and findings to the arteriovenous fistula found at arteriography, as she was an elderly female with a history of 1 episode of congestive heart failure 2 years prior to admission. Since the tumor was not removed, there was no opportunity to follow her postoperatively for regression of symptoms. Cases III and IV showed no cardiovascular manifestations.

It is apparent then that cardiovascular

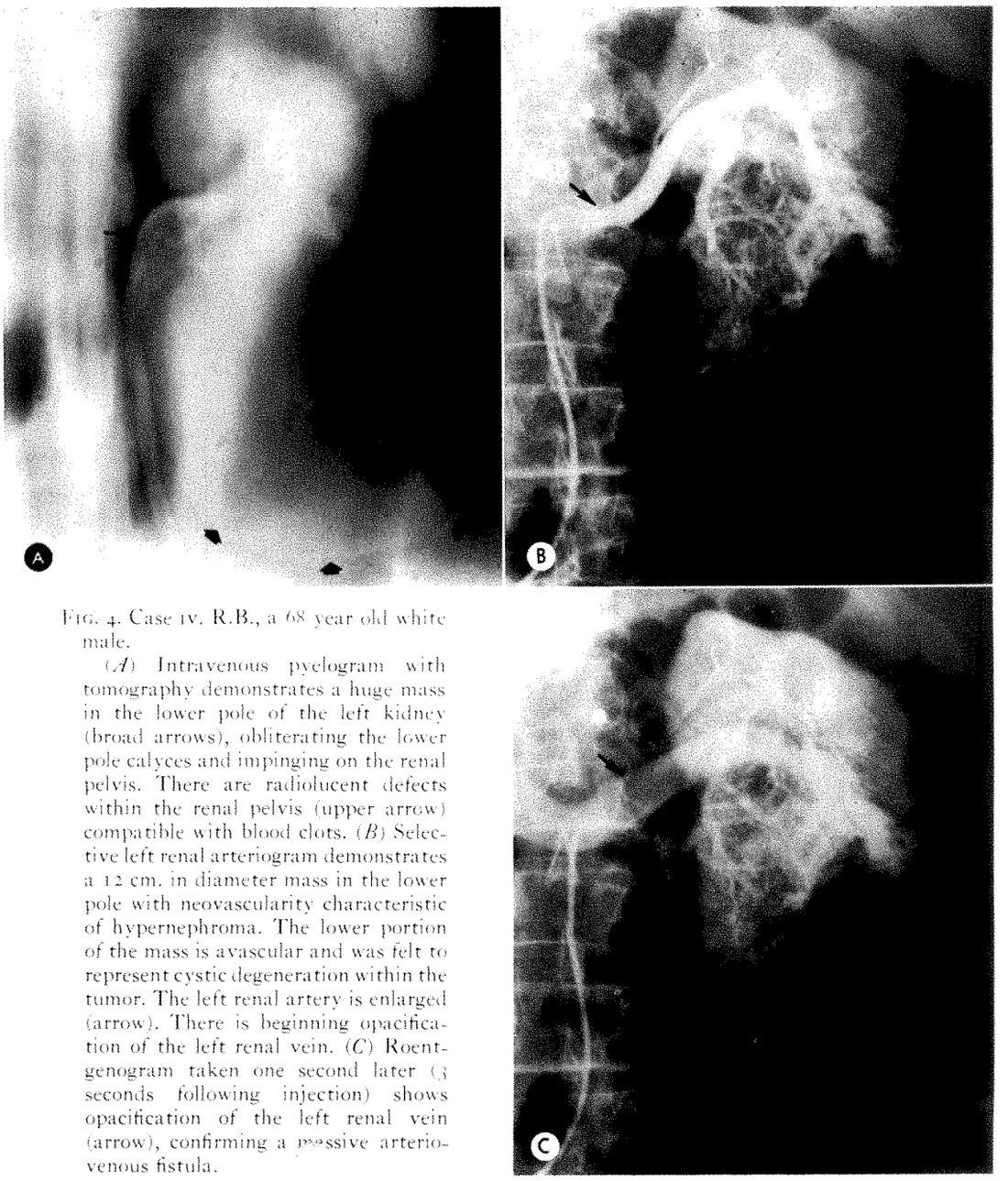


FIG. 4. Case IV. R.B., a 68 year old white male.

(*A*) Intravenous pyelogram with tomography demonstrates a huge mass in the lower pole of the left kidney (broad arrows), obliterating the lower pole calyces and impinging on the renal pelvis. There are radiolucent defects within the renal pelvis (upper arrow) compatible with blood clots. (*B*) Selective left renal arteriogram demonstrates a 12 cm. in diameter mass in the lower pole with neovascularity characteristic of hypernephroma. The lower portion of the mass is avascular and was felt to represent cystic degeneration within the tumor. The left renal artery is enlarged (arrow). There is beginning opacification of the left renal vein. (*C*) Roentgenogram taken one second later (3 seconds following injection) shows opacification of the left renal vein (arrow), confirming a massive arteriovenous fistula.

manifestations are not always associated with this entity. Out of the 20 cases now reported in the literature, only 8 had definite cardiovascular manifestations. Whether they are present or not depends on: (1) the duration of time the fistula has been present; (2) the size of the shunt in relation to its feeding artery and draining vein;[7] and (3) the status of the cardiovascular system prior to the occurrence of the fistula. It is reasonable to expect then that all hypernephromas with massive arteriovenous fistula would not have cardiovascular signs and symptoms, as the fistula may be of re-

cent occurrence and the diagnosis obtained and treatment performed before hemodynamic changes have had time to develop.

ROENTGENOGRAPHIC FEATURES

In order to qualify as a massive arteriovenous fistula, as opposed to the small peripheral arteriovenous fistulas commonly seen in hypernephroma, certain roentgenographic criteria must be met. According to Bosniak,[3] there must be considerable opacification of the renal vein within $\frac{1}{2}$-1 second following opacification of the renal artery, or the renal vein and the inferior vena cava must be opacified while there is still contrast medium within the aorta. The normal opacification of the inferior vena cava occurs at approximately 8 seconds following injection, whereas in massive arteriovenous fistula it occurs at 4 to 5 seconds. These criteria were fully met in the 4 cases presented here. In addition, pathologic vessels characteristic of hypernephroma were seen, differentiating these cases from arteriovenous fistulas of other causes.

Diagnostic difficulty was encountered in only 1 case (Case II). The initial impression was that this was a congenital arteriovenous malformation, due to the wide tortuous vessels seen on arteriography. However, the mass bulging from the lateral aspect of the lower pole with associated displacement and distortion of the lower pole calyces plus the small pathologic vessels seen in this area were irrefutable evidence for tumor. Boijsen and Kohler[2] list "pathological" vessels and signs of an expanding process as the 2 most reliable features in distinguishing congenital arteriovenous malformations from hypernephroma with massive arteriovenous fistula.

Another interesting feature was the ureteral notching on the involved side seen in 2 cases (Case II, Fig. 2*A*; and Case III, Fig. 3*A*). On arteriography, this is seen to be caused by hypertrophy of the upper ureteral arteries. The normal blood flow in the ureteral arteries is reversed and they contribute to feeding the shunt, and thus become dilated due to the increased flow. Bosniak[3] was the first to report this finding in conjunction with hypernephromas with massive arteriovenous fistula.

PATHOLOGIC FEATURES

The mechanism of massive arteriovenous fistula in association with hypernephroma is invasion of the main renal vein by the tumor with subsequent erosion into a renal artery. The pathologic findings in the 2 operated cases in our series would support this. In both cases there was definite extension of the tumor into the main renal vein with involvement of the major vessels about the hilum.

SUMMARY

Four cases of hypernephroma with massive arteriovenous fistula are reported.

A review of the literature together with our cases show that cardiovascular manifestations are not always associated with this entity at the time of discovery, as has been previously stressed in the literature. The factors thought to be responsible for this are mentioned.

The clinical, roentgenologic, and pathologic features of our 4 cases are discussed.

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BILATERAL HYPERNEPHROMA*

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ALTHOUGH bilateral Wilms' tumor has been shown to occur with a frequency of 3.6 per cent,[6] bilateral hypernephroma is much less frequently encountered.

The first case of bilateral renal cell carcinoma was described in 1910 and a review of the English literature by Small *et al.*[7] in 1968 revealed 17 previously reported "acceptable" cases to which they added 1 of their own. In the interval since that review, 2 additional cases have been reported.[3,4]

Of these 20 cases, only 3 underwent angiographic evaluation of any kind and only 1 previous case had selective renal arteriography.[4]

REPORT OF A CASE

C.S., a 53 year old Puerto Rican woman, was admitted to the St. Luke's Hospital Center with a 4 day history of dysuria and a temperature of 102° F. There was no history of flank pain or hematuria. However, the patient had suffered back pain intermittently over a 2 year period.

Physical examination revealed an obese woman in no distress. No abdominal or flank masses were palpable. There was right costovertebral angle tenderness. The remainder of the examination was within normal limits.

A preliminary supine roentgenogram of the abdomen (Fig. 1) showed a rounded mass in the lower pole of the left kidney. Additionally, several areas of calcification were seen superimposed on the right lateral renal border. Roentgenograms obtained during an intravenous pyelography (Fig. 2, *A* and *B*) confirmed the presence of a left lower pole mass, and the right posterior oblique projection showed that the calcification seen over the right renal border laterally on the preliminary roentgenogram was associated with a right renal mass which projected anteriorly.

A midstream retrograde femoral aortogram (Fig. 3) showed one renal artery on each side. A large, well circumscribed mass in the left lower pole was seen, which demonstrated rich neovascularity. A questionable tumor stain was seen on the right in the region of the partially calcified right renal mass. Selective renal arteriography was carried out on both sides. On the left (Fig. 4, *A* and *B*), the mass in the lower pole and its tumor vessels were demonstrated to better advantage. On the right (Fig. 5, *A* and *B*), a definite tumor blush was identified along the lateral border, which had not been clearly seen on the midstream injection. Based on the angiographic findings, the preoperative diagnosis was bilateral hypernephroma.

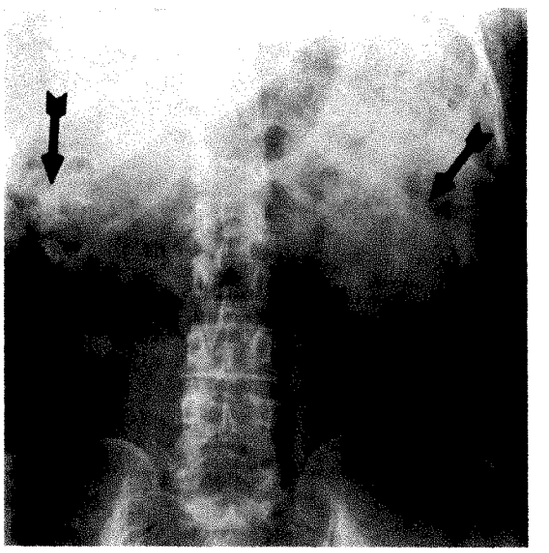


FIG. 1. Supine roentgenogram of the abdomen obtained prior to intravenous pyelography shows a mass in the plane of the lower pole of the left kidney (double arrows) and several amorphous calcifications associated with the right lateral renal border (single arrow).

Initial surgery consisted of biopsy of the right renal mass, followed by left lower pole heminephrectomy. The pathology report was bilateral hypernephroma. The histology was different on the 2 sides (Fig. 6, *A* and *B*), with the right cancer showing cuboidal cells with clear cytoplasm and the left cancer showing cell clusters with eosinophilic cytoplasm, hyperchromatic nuclei and many multinucleated giant cells. After adequate functioning of the

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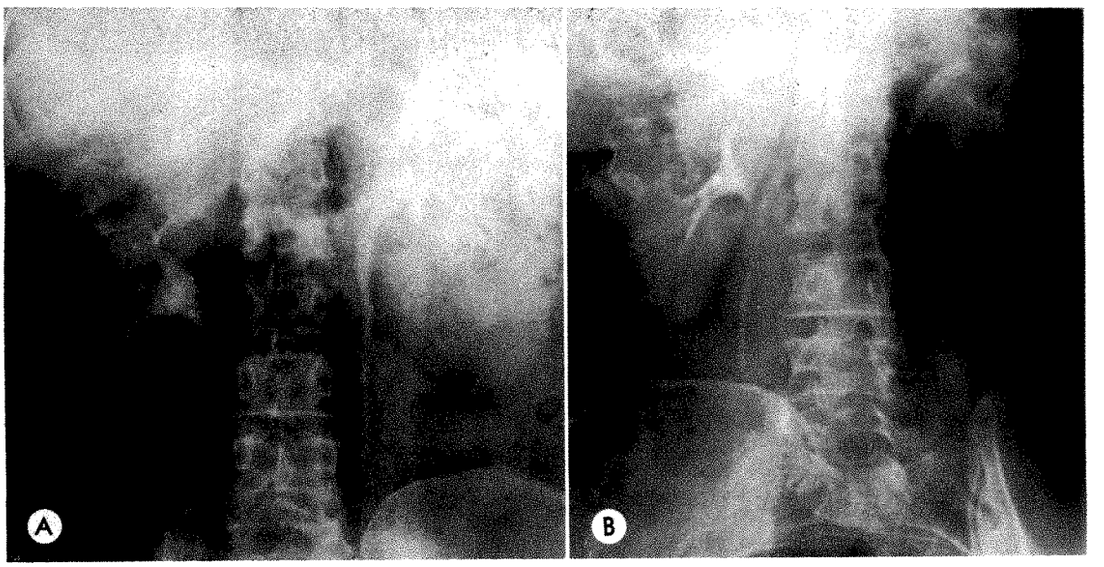


Fig. 2. (*A*) Intravenous pyelogram. The left lower pole mass is seen to better advantage. The calcifications on the right are again seen, and there is a suggestion of a mass in this area as well. (*B*) The right posterior oblique projection confirms the presence of a right renal mass with calcification. The mass is seen to project anteriorly.

left upper pole had been established, a right radical nephrectomy was performed.

DISCUSSION

Although renal cell carcinoma, metastatic to the contralateral kidney, is seen with some frequency at autopsy, the simultaneous occurrence of bilateral hypernephroma has been reported with great rarity.

Over the years, various criteria have been suggested for the diagnosis of bilateral primary tumors. Initially, it was suggested that each tumor should have different histologic structure, individual metastasis and different points of origin. These criteria are obviously too strict, as a patient could succumb from metastatic disease from one primary before the other tumor metastasized.

Obviously, no criteria exist which are completely satisfactory for distinguishing bilateral primary renal cell carcinoma from unilateral tumors metastatic to the opposite side.

It is suggested that the following criteria may prove of value: (1) the tumors should preferably occur simultaneously. Many cases have been reported with renal cell carcinoma in the contralateral kidney months to years after nephrectomy for a primary tumor. Many of these cases undoubtedly represent metastatic disease; (2)

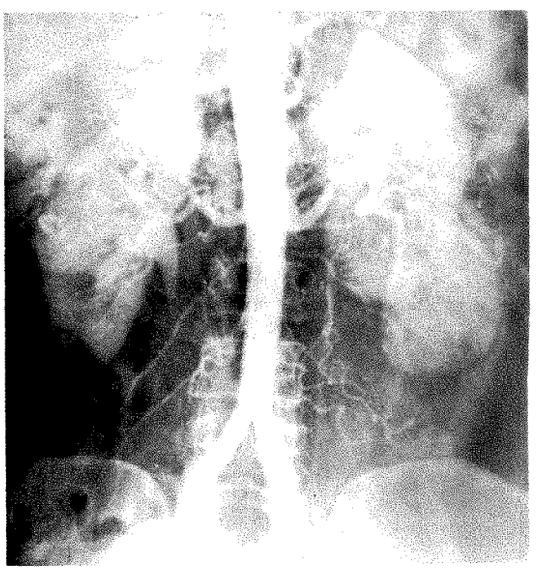


Fig. 3. A midstream aortic injection of contrast medium shows a large well circumscribed mass with rich neovascularity in the left kidney. There is a questionable tumor blush in the right kidney.

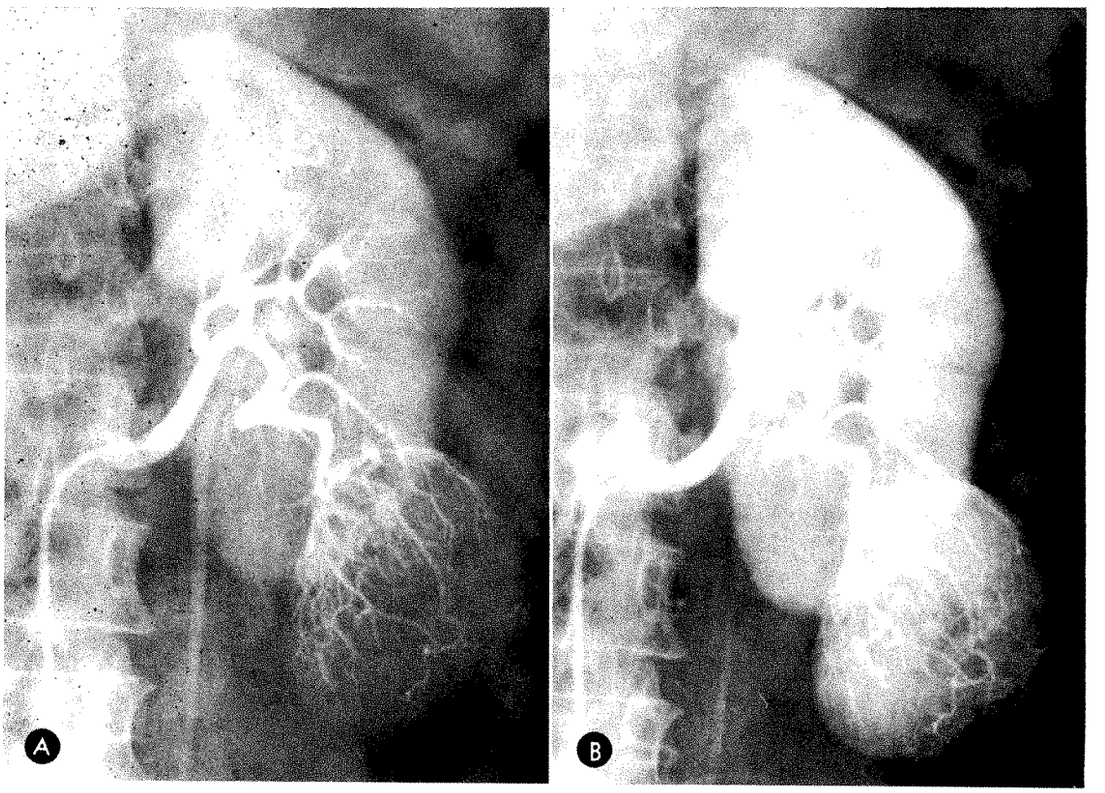


FIG. 4. Selective left renal arteriograms. (*A*) Early arterial phase. (*B*) Late arterial phase. The tumor mass in the left lower pole and its neovasculature are seen to better advantage.

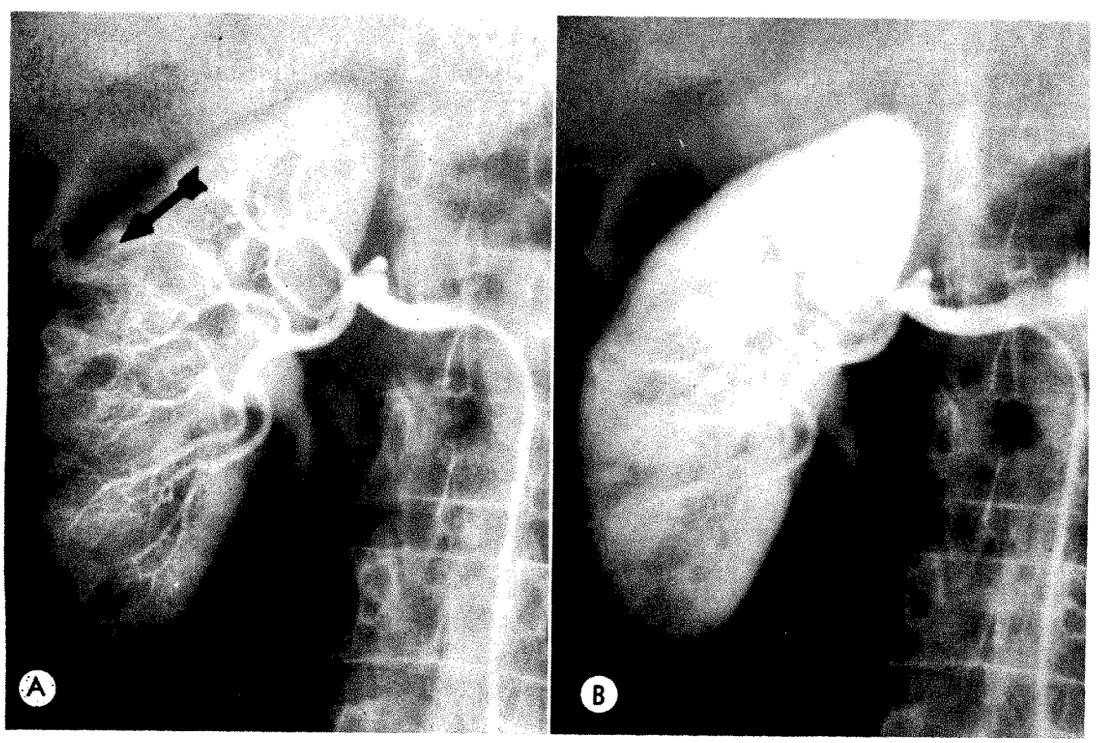


FIG. 5. Selective right renal arteriograms. (*A*) Early arterial phase. The presence of tumor stain (arrow) and neovascularity is confirmed on the selective injection. (*B*) Late arterial phase.

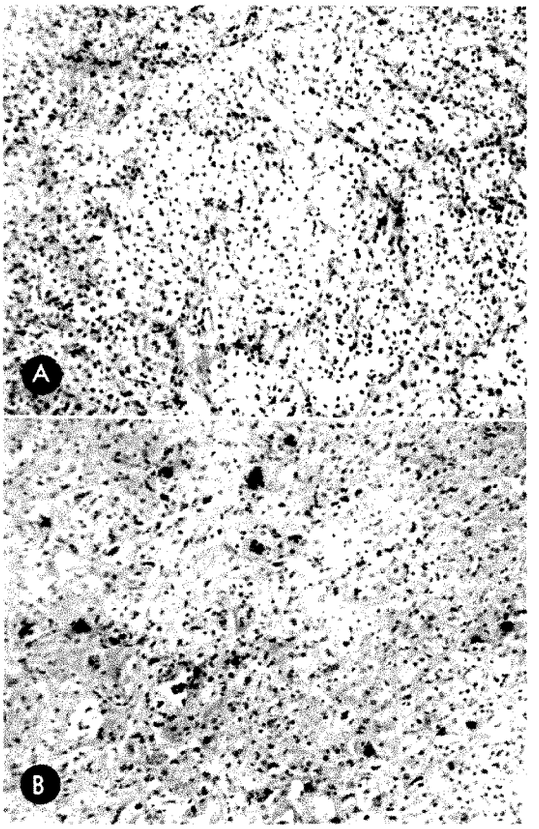


Fig. 6. (*A*) The right renal tumor demonstrates a predominance of cuboidal cells with clear cytoplasm (176×). (*B*) The left renal tumor shows many multinucleated giant cells and cell clusters with eosinophilic cytoplasm (176×).

there should be only 1 tumor in each kidney. Multiple lesions suggest metastasis; (3) each tumor should show at least partial encapsulation; and (4) the basic histology should be different in each lesion.

The age and sex characteristics of patients with bilateral hypernephroma are interesting. The male preponderance is even greater in bilateral hypernephroma than in unilateral disease. Of the 21 cases considered in this paper, 17 have been in males. The lesion also tends to occur in a somewhat younger age group, usually in the fifth decade; unilateral lesions are usually seen in the seventh decade.[5]

Finally, in only a few of the 20 cases prior to this report was the diagnosis of bilateral hypernephroma entertained preoperatively. Now that renal masses are being investigated with nephrotomography, renal arteriography, venacavography and renal venography when appropriate, we may expect to see more reports of bilateral hypernephroma diagnosed preoperatively.

SUMMARY

A case of simultaneous bilateral hypernephroma is reported and the characteristics of the 20 cases previously reported in the English literature are discussed.

The criteria of value in distinguishing bilateral hypernephroma from a unilateral primary lesion with contralateral renal metastasis are reviewed.

More widespread use of renal angiography should lead to an increase in the preoperative diagnosis of the entity.

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ANGIONEPHROTOMOGRAPHY AND SUBTRACTION*

RELATIVE VALUE IN RENAL MASS LESIONS

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SELECTIVE renal arteriography, despite its limitations,[6] is widely used in the evaluation of renal mass lesions.[2,7] With or without the aid of ultrasonography[4] and percutaneous puncture,[5] the selective renal arteriogram will often establish the diagnosis and influence patient management. It is therefore mandatory to try to extract

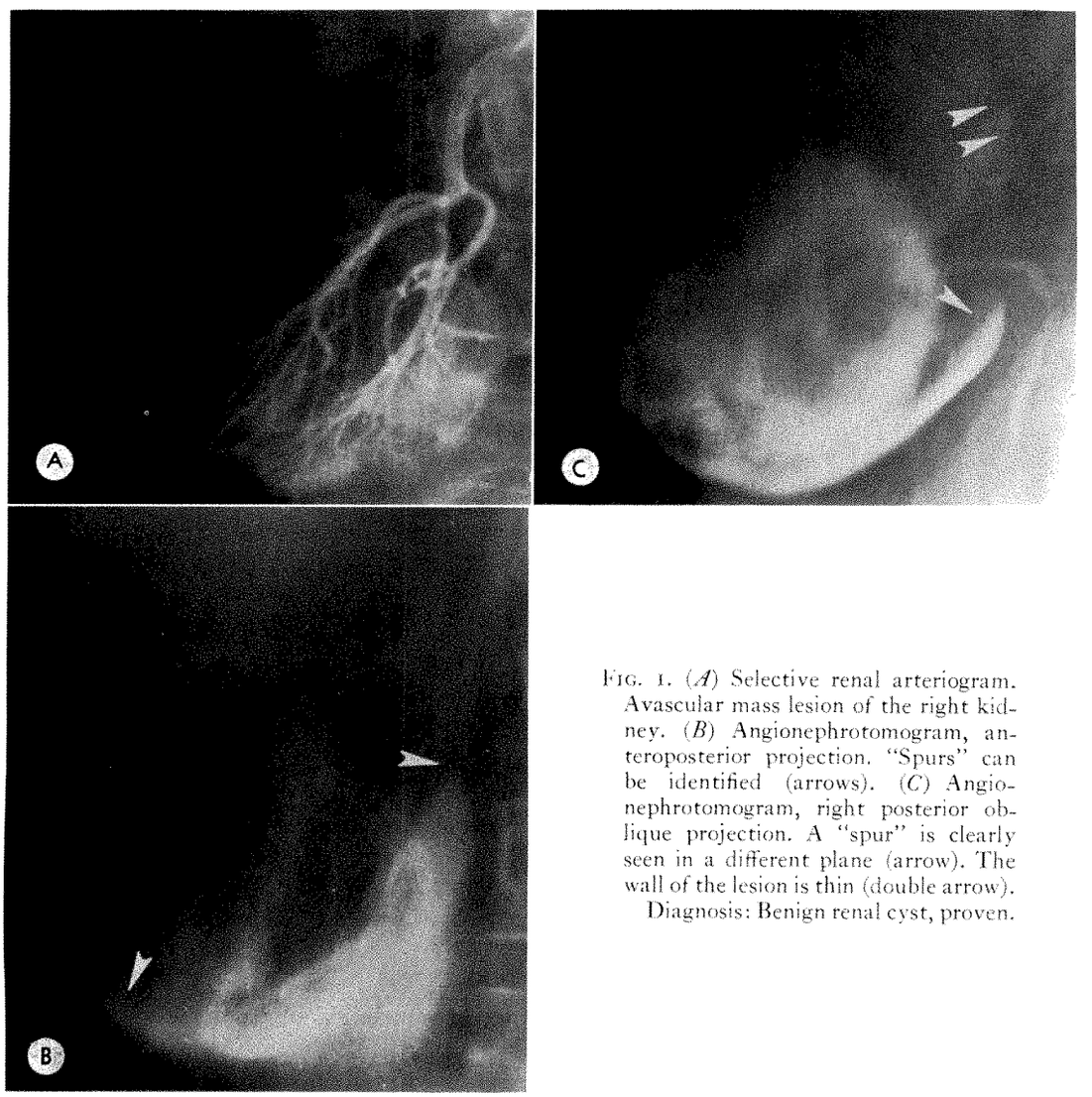


FIG. 1. (*A*) Selective renal arteriogram. Avascular mass lesion of the right kidney. (*B*) Angionephrotomogram, anteroposterior projection. "Spurs" can be identified (arrows). (*C*) Angionephrotomogram, right posterior oblique projection. A "spur" is clearly seen in a different plane (arrow). The wall of the lesion is thin (double arrow).
Diagnosis: Benign renal cyst, proven.

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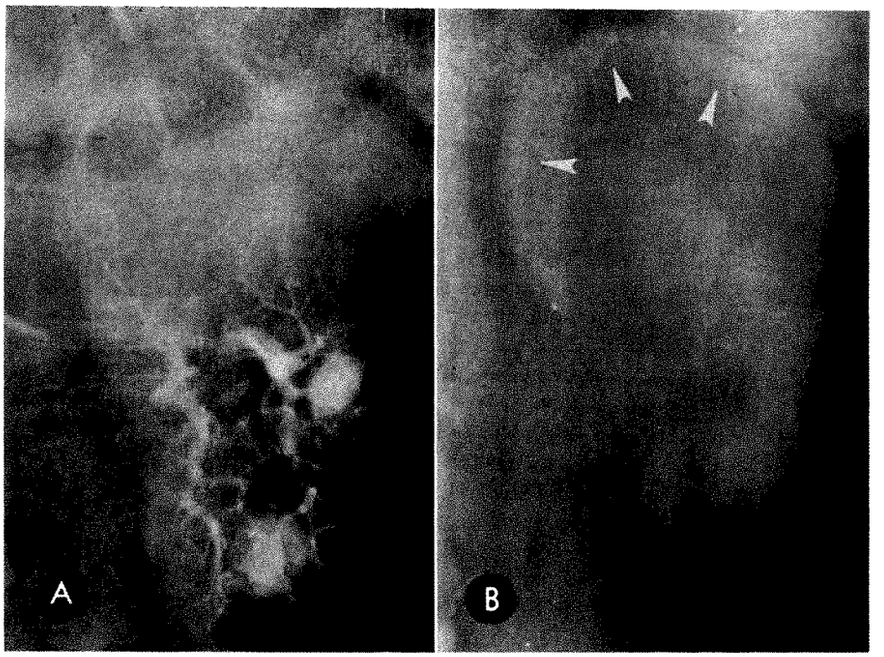


Fig. 2. (*A*) Selective renal arteriogram. Avascular mass lesion of upper pole of the left kidney. (*B*) Angionephrotomogram. The wall of the lesion is thick (arrows).
Diagnosis: Proven necrotic hypernephroma.

from the angiogram as much information as possible in order to arrive at a correct diagnosis.

With this in mind, we have routinely performed angionephrotomography and subtraction in cases where a renal mass was not obviously a vascular carcinoma by selective angiography.

METHOD

Angionephrotomography is a simple procedure, performed at the time of renal angiography, without additional risk to the patient.

The purpose is to obtain tomograms of the kidney involved during the arterial phase and the intense nephrographic phase which follows the injection of contrast material selectively into the renal artery: 8.0 to 10.00 ml. of meglucamine diatrizoate is totally injected for this purpose. At first, 4.0 ml. is rapidly injected and, after 2–3 seconds delay, the remaining portion of contrast medium is introduced simultaneously with the first tomographic exposure. More tomograms are then obtained in appropriate projections.

Selected roentgenograms from the angiogram and angionephrotomogram are submitted to second order photographic subtraction, utilizing routine methods for the masks, and high contrast film or photographic paper for the final subtraction.[3]

RESULTS

Angionephrotomography was found to be useful when evaluating for "spurs" and thickness of the lesion wall. By obtaining tomograms at appropriate levels and in different projections, a "spur" can be identified in at least 2 planes and the thickness of the lesion wall can be appreciated (Fig. 1, *A–C*; and 2, *A* and *B*).

Subtraction, on the other hand, was proven very valuable in demonstrating tumor vessels which could not be identified on the conventional or post epinephrine angiogram (Fig. 3, *A–E*). Furthermore, the application of subtraction in calcified renal masses was proven to be very helpful.

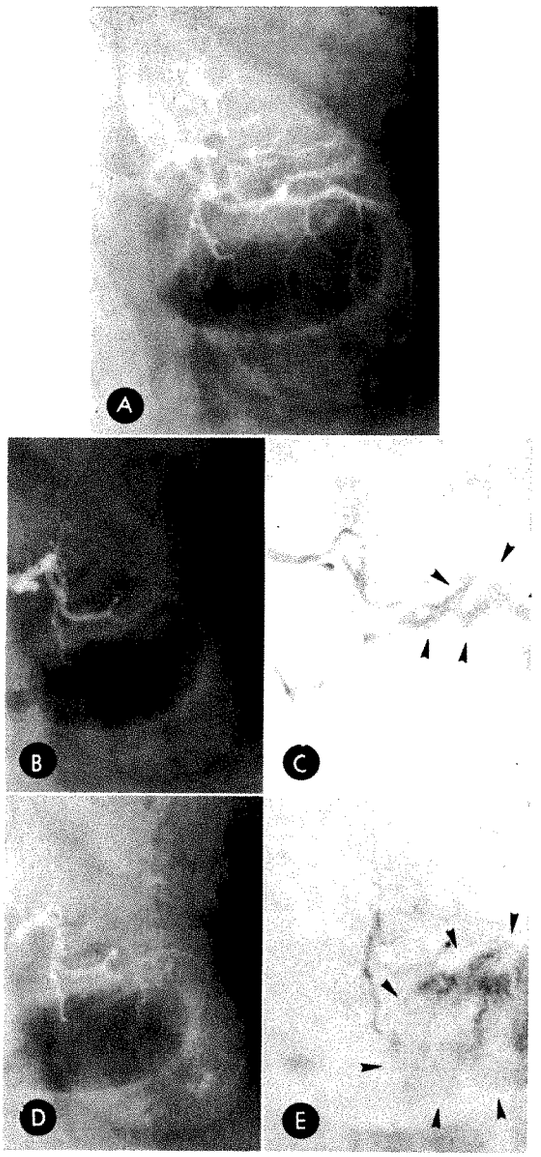


FIG. 3. (*A*) Selective renal arteriogram. Avascular mass lesion of lower pole of the left kidney. (*B* and *C*) Post epinephrine renal arteriogram. Roentgenogram exposed at 4.5 seconds (*B*) and subtraction of the same (*C*). Tumor stain (arrows) can be identified only in the subtraction study (arrows). (*D* and *E*) Post epinephrine renal arteriogram. Roentgenogram exposed at 9.5 seconds (*D*) and subtraction of the same (*E*). Intense tumor stain (arrows) can be recognized in the subtraction study.

Diagnosis: Avascular necrotic hypernephroma, confirmed at surgery.

When calcium was eliminated by subtraction, tumor vessels and stain were readily identified (Fig. 4, *A–C*).

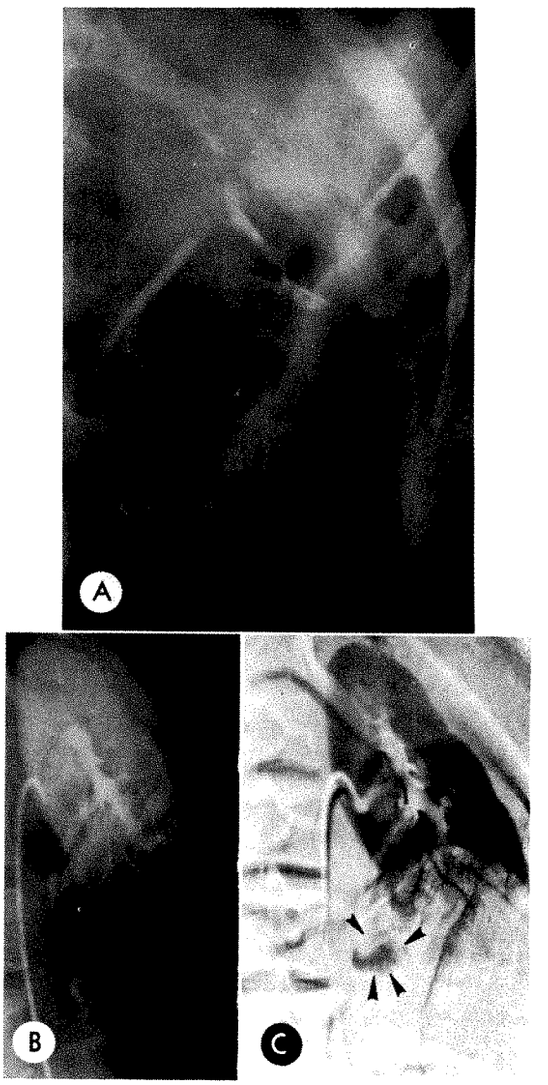


FIG. 4. (*A*) Intravenous pyelogram. There is a calcified mass of the lower pole of the left kidney. (*B* and *C*) Selective renal arteriogram (*B*) with subtraction (*C*). Although the mass is avascular, tumor stain (arrows) is identified when the calcium is eliminated by subtraction.

Diagnosis: Avascular hypernephroma, confirmed at surgery.

DISCUSSION

The criteria for differentiating a benign cyst from an avascular tumor on nephrotomography and angiography depend upon the presence of a thin wall[1] and a "beak-shaped" elevation of the kidney parenchyma around the space-taking process.[7] While angiography *per se* may sometimes give the

information necessary to conclude that a renal mass is indeed a cyst and not an avascular tumor, the angionephrotomogram with the biphasic visualization of the arterial and nephrographic phase may be of considerable value in delineating the anatomy of the lesion, the wall and the presence or absence of "spurs."

Photographic subtraction of the angiogram by eliminating extraneous superimposed shadows or calcifications may be of further help in detecting the presence or absence of abnormal vessels or tumor stain. Obviously, percutaneous puncture of the lesion, while of considerable diagnostic value,[5] is possibly not an ideal procedure in those lesions where the radiologic suspicion, on the basis of angiography, leans toward a relatively avascular tumor. In this situation, angionephrotomography and subtraction may delineate the pathology without the need to puncture a tumor percutaneously.

SUMMARY

Angionephrotomography and subtraction may be useful adjuncts to selective renal arteriography in the evaluation of renal mass lesions.

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EVALUATION OF ULTRASONIC B-MODE SCANNING IN THE DIAGNOSIS OF RENAL MASSES*

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B-MODE ultrasonic scanning is becoming an important part of preoperative evaluation of renal mass lesions. It gives more information than simple A-Mode Ultrasound, is inexpensive in comparison to angiography, and most important, it is an atraumatic and noninvasive method.

Because of these advantages this study was undertaken to evaluate B-Mode scanning in the diagnosis of renal mass lesions.

The study was planned to determine both the diagnostic accuracy of ultrasonic B-scanning in renal mass lesions and its role in the evaluation of patients with a renal mass.

MATERIAL AND METHOD

Forty-seven patients with renal masses demonstrated at intravenous urography were included in the study. All had both renal angiograms and ultrasonic B-scans (Table I).

Confirmation of the diagnosis was obtained by cyst puncture, angiography and/or surgery (Table II). All masses having the angiographic characteristics of neoplasm, and all masses in which malignancy could not be confidently excluded were explored. About half of the lesions thought to be cysts were submitted to cyst puncture.

In the early part of the study the radiologists performing and interpreting the scans were given no information until after the scan was interpreted. However, the time required to produce an adequate scan under these circumstances, and the difficulties of recognizing smaller lesions caused us to modify this procedure. In the latter part of the study the plain roentgenograms and intravenous urograms were reviewed by the ultrasonologist before performing the scan. All other information was withheld until after the interpretation of the scan. Ultrasonic examinations were performed with the patient prone. Transverse B-scans were performed in all patients, longitudinal and oblique B-scans in many. A Picker ultrasonoscope was used for all ultrasonic scans. An ultrasonic A-mode study of the lesion was performed in many patients once the precise position of the lesion was defined by B-scanning.

TABLE I

MATERIAL

Total number of patients	47
Number of cysts	20
Number of essentially normal kidneys	11
Number of hydronephroses	4
Number of solid tumors	12

RESULTS

Twenty patients had cysts. Three of these were not detected by B-scanning. One of these, early in the series, was 3 cm. in diameter. The other 2 were less than 2 cm. in diameter. No cyst was called a tumor.

Two of 12 tumors were called cystic on B-scan. Both of these had features which, in retrospect, and with greater experience could have led us to a diagnosis of a solid lesion (Fig. 1, *A–D*).

TABLE II

BASIS OF DIAGNOSIS OF CYSTS

Diagnosed by puncture and cytology	10
Diagnosed by surgery or necropsy	2
Diagnosed by angiography	8

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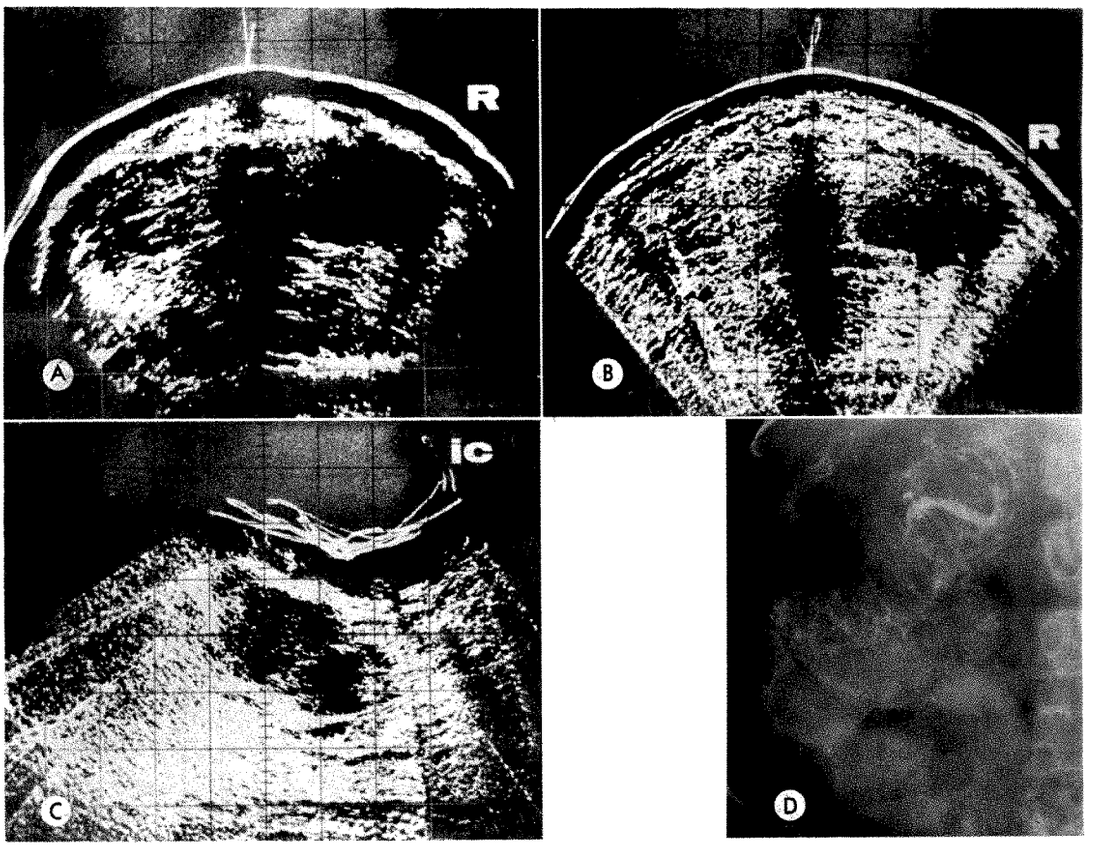


FIG. 1. Hypernephroma (R). This tumor was misdiagnosed as a cyst ultrasonically. (*A*) Transverse scan at low gain shows echo-free interior and well defined deep margin with good transmission. (*B*) Transverse scan at higher gain and (*C*) longitudinal scan show internal echoes in the R upper pole tumor which in retrospect give the correct diagnosis. I.C. indicates iliac crest. (*D*) Tumor vascularity seen on angiography.

Conversely, 1 renal cell carcinoma was avascular at angiography and was interpreted as a benign cyst (Fig. 2, *A–C*). Another patient had angiographic changes suggestive of an inflammatory lesion, but neoplasm could not be excluded angiographically. Both had ultrasonic characteristics of a solid lesion. Accuracy of B-scan diagnosis is summarized in Table III.

In 11 patients in which angiography demonstrated essentially normal kidneys (*i.e.*, no mass lesion), ultrasonic B-scan did not produce any false positive results.

Four patients had hydronephrosis, all diagnosed correctly by ultrasonic B-scan. One of these, a 15 year old boy with poor renal function, presented with a left upper quadrant mass. Intravenous pyelography failed to visualize the kidneys. Ultrasonic B-scanning correctly identified the mass as massive hydronephrosis of the left kidney. This was confirmed at angiography and at surgery (Fig. 5, *A* and *B*).

DISCUSSION

The results of this series indicate that good accuracy can be achieved in distinguishing ultrasonically between cystic and solid renal masses. However, there are certain important limitations which must be observed if a high level of accuracy is to be maintained.

The criteria for the diagnosis of cystic lesions by ultrasound are:

1. The interior of the lesion must be echo free at both low and high gain settings. An

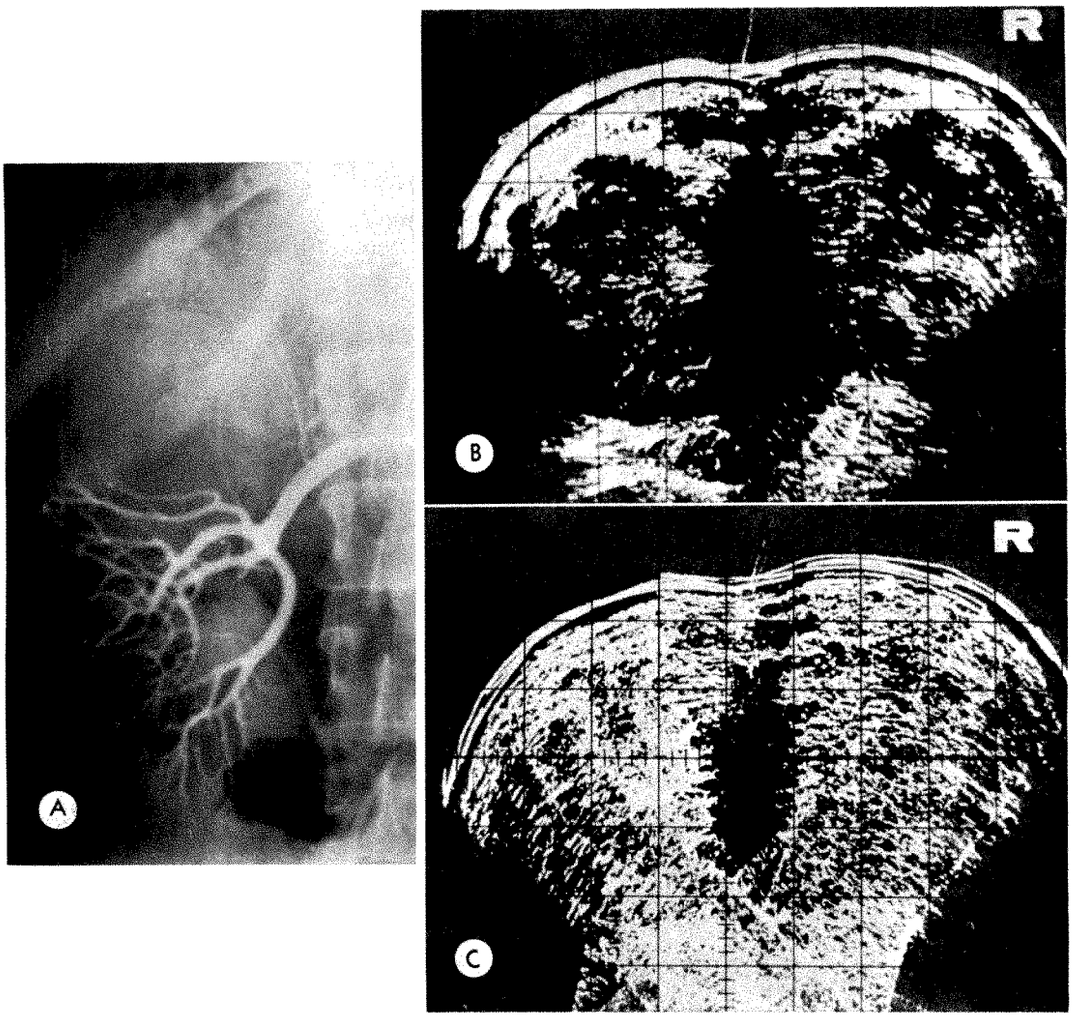


FIG. 2. Papillary adenocarcinoma of R kidney. (*A*) Angiographically this R upper pole mass was avascular and was interpreted as a cyst. (*B*) Low gain B-scan showed a bulky R kidney with poorly defined margins and some internal echoes. (*C*) High gain B-scan shows filling in of the area to the same extent as the contralateral normal kidney.

exception to this, however, is sometimes seen. Echoes may be seen in the more superficial parts of a cystic lesion, due presumably to reverberations from overlying structures, particularly where ribs overlie a cystic lesion of the upper pole of the kidney. These artifacts can be recognized by the fact that they remain superficial, in constant relationship to the scanner rather than in constant relationship to the cyst.

2. The lesion must transmit the sound well so that echoes are obtained from structures deep to the lesion.

3. A sharply delineated deep wall must be seen[1,2,4,6,9] (Fig. 3, *A* and *B*).

If any of these criteria are not met, the diagnosis of a cystic lesion must be in doubt.

Solid lesions, on the other hand, have internal echoes at higher gain settings and have poorly defined deep walls (Fig. 4, *A* and *B*). When the nature and precise position of the lesion has been decided as far as possible on the basis of its B-mode appearances, confirmation may be obtained from the A-mode study, the value of which has

been discussed by others.[4] Unless these criteria are rigidly adhered to, it is possible to misdiagnose certain solid lesions as cystic (Fig. 1, *A–D*). Any lesion that does not have characteristics that are clearly cystic should be considered solid. There is no implication as to whether the lesion is benign or malignant in this statement, except that cystic lesions are usually benign.

Ultrasound B-scanning is at present unreliable in detecting lesions that are smaller than 2 cm. or perhaps 3 cm. in diameter.[4] Furthermore, the technique is generally unable to distinguish with certainty between a small solid tumor and the solid tissue of a normal kidney.[4] Also, detection of a lesion may be laborious, even if it is moderately large, when its site is unknown. For these reasons it is apparent that ultrasonic B-scanning has no place as a screening procedure. We differ here from Damascelli *et al.*[3] who suggest its use as such.

In patients in whom the ultrasonic B-scan diagnosis is uncertain, it is useful to compare the ultrasonic characteristics of the lesion with those of a known reference organ. This aids in determining the most satisfactory gain setting for examining an organ or a lesion. While use of standardized gain settings are helpful, we have found that the appearance of an ultrasonic B-scan varies greatly from patient to patient with fixed gain settings and even from minute to minute in the same patient. One variable difficult to control is the amount of mineral oil or other coupling agent used on the skin. The motion of the transducer and the number of passes of the transducer over the lesion all have effects on the appearance of the image and are variables that are difficult to control. By arranging the position and angulation of the scanner in such a way that the plane of the scan passes through both the lesion under investigation and an organ of known ultrasonic properties such as bladder, liver, spleen, contralateral kidney or even the normal part of the involved kidney, it is possible to include parts of the lesion and parts of the reference organ in

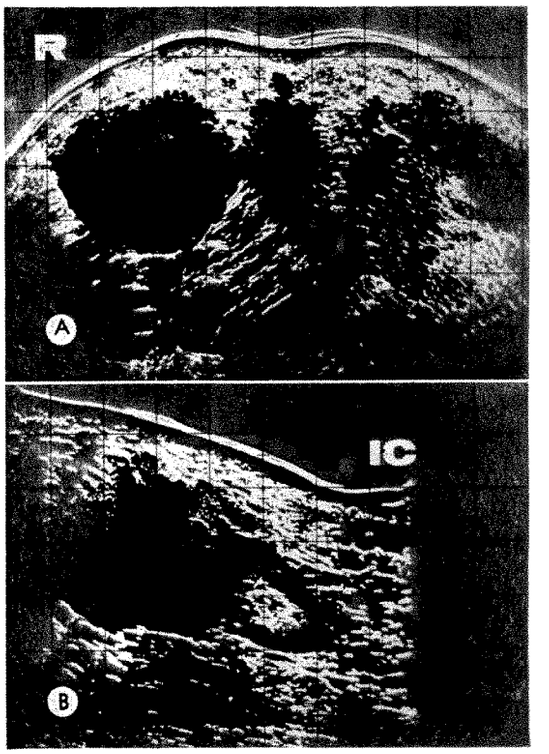


Fig. 3. Example of a cystic renal mass in (*A*) transverse and (*B*) longitudinal scans. Note the echo-free interior, well defined deep wall and transmission of sound from deeper structures. I.C. indicates iliac crest.

Table III

ACCURACY OF B-SCAN DIAGNOSIS

1. *Cysts*	
Total	20
Number correctly identified	17
Number missed	3
(One 3 cm. in diameter, the other 2 both less than 2 cm. in diameter)	
Number called solid	0
2. *Malignant tumors*	
Total	12
Number called solid	10
Number incorrectly called cystic	2
(Both appeared solid in retrospect)	
3. *Essentially Normal Kidneys*	
Total	11
Number correctly diagnosed	11
(No cyst, no discrete mass)	
4. *Hydronephroses*	
Total	4
Number correctly diagnosed	4

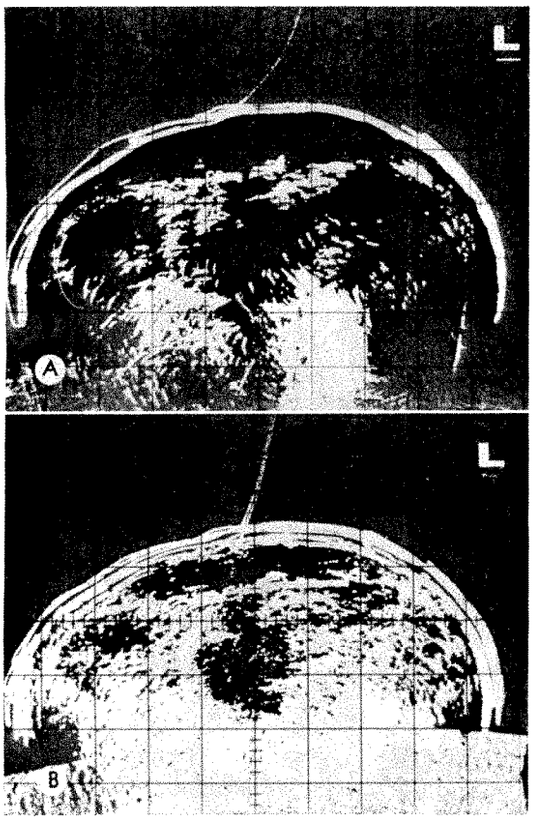


FIG. 4. Example of a solid L renal mass (hypernephroma) at (*A*) low and (*B*) high gain settings, in transverse scans at the same level. Note the occasional internal echoes at low gain which are more prominent at high gain. Echoes from the deep wall of the mass are attenuated; hence, it is less well defined.

the one picture. By keeping the speed of motion of the transducer head and the other variables as nearly constant as possible throughout the performance of a view, the appearance of the reference organ and of the lesion becomes roughly comparable (Fig. 6). The assumption is made that the reference organ is normal. Because of this, caution must be exercised if the results appear discordant or there is a history or physical signs suggestive of disease in the reference organ. A full bladder is probably the best reference standard, but it may not be possible to include the bladder and the lesion under study in the one cut.[3]

SUGGESTED ROLE OF ULTRASOUND B-SCANNING IN EVALUATION OF PATIENTS WITH RENAL MASSES

The direct puncture of renal cysts and examination of the aspirated fluid is a highly accurate method of defining the benign nature of cysts.[7,8] In many institutions the use of cyst puncture has done away with the necessity for surgical exploration of benign cysts. Even urologists who accept cyst puncture as a definite diagnostic approach are hesitant to have needles placed in tumors. In these institutions angiograms are generally performed to separate cystic and neoplastic lesions. Those masses having angiographic characteristics of cysts are then punctured and those having characteristics of tumor are explored. Ultrasonic B-scanning can serve

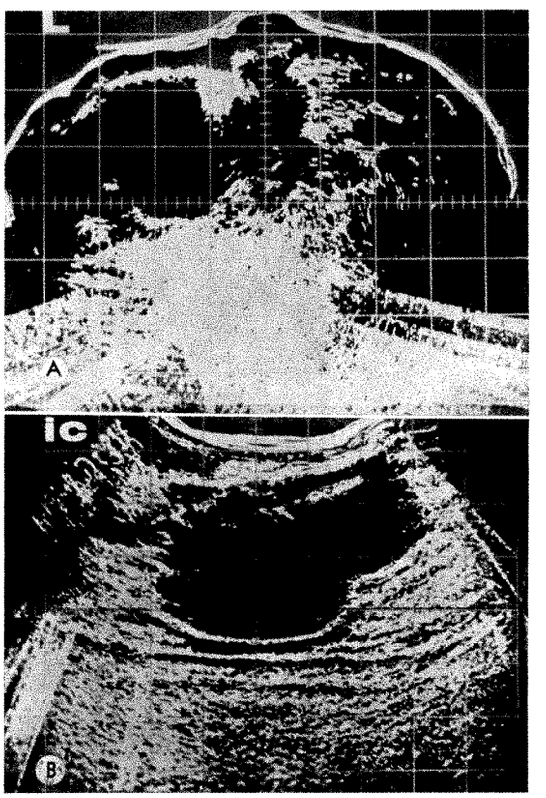


FIG. 5. Massive L hydronephrosis. (*A*) Transverse scan and (*B*) longitudinal scan show a fluid filled mass in the L renal area. I.C. indicates iliac crest.

as a noninvasive and inexpensive substitute for angiography in differentiating between cystic and solid renal masses.

Thus, when a renal mass is detected by intravenous urography, the next procedure should be an ultrasonic B-scan. If the lesion is cystic, a needle puncture and aspiration should be done to confirm the benign nature of the cyst. Hydronephrosis, if not already suggested as a diagnosis on the basis of its ultrasonic B-scan appearances[1-5] (Fig. 5, *A* and *B*), will be detected at this point. If the lesion is indeterminate or solid, angiography should be done to confirm its malignant nature, and to define the blood supply, to get an indication of the extent of the lesion and to detect the presence of liver metastases prior to exploration. With this approach, many needless renal angiograms will be avoided in patients with benign cysts, and at the same time very few neoplasms will be punctured. In the approximately 10 per cent of patients in whom a misdiagnosis of cyst or tumor is made by ultrasonic B-scanning, the patient will still have the correct diagnosis made at the appropriate follow-up examinations. Cysts misdiagnosed as neoplasms will have angiography and exploration. Tumors which are diagnosed as cysts will be punctured and their solid nature detected. They then can have angiography and exploration. Figure 7 summarizes the suggested plan of work-up.

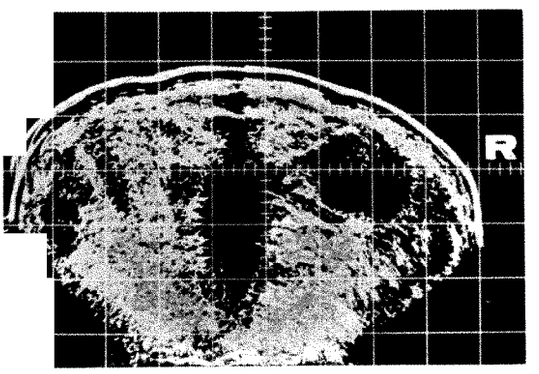


FIG. 6. Right renal cyst is compared with liver seen laterally in the same scan. The group of internal echoes seen in the near side of the cyst are an example of artifact, and do not indicate that the lesion is solid.

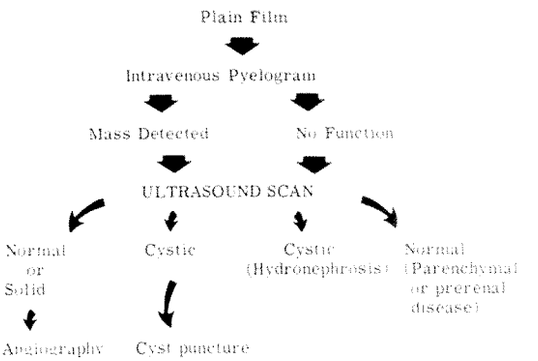


FIG. 7. Suggested plan for the work-up of a patient with a renal mass.

SUMMARY

1. Ultrasonic B-scanning is useful in differentiating between cystic and solid renal masses when the presence of a mass is known from plain roentgenograms or intravenous pyelograms, and the mass is known to be greater than 2 to 3 cm. in diameter.

2. Ultrasonic B-scanning is not a useful screening procedure.

3. Criteria for distinguishing a cyst from a solid lesion with ultrasonic scanning should be rigidly adhered to and all doubtful lesions should be presumed solid. An apparently normal renal echogram in the presence of a mass seen at intravenous pyelography suggests a solid lesion.

4. Comparison of the characteristics of the lesion with those of a reference organ avoids errors due to improper setting of the gain controls.

5. Ultrasonic B-scanning is useful in delineating hydronephrosis, when renal function is poor.

6. Ultrasonic B-scanning should follow the discovery of a renal mass lesion on intravenous pyelography and should precede either cyst puncture or renal angiography.

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ULTRASONIC DIAGNOSIS OF WILMS' TUMORS*

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OF ALL the publications on tumor diagnosis with ultrasound tomography and the A-scope technique, the great majority are in the fields of gynecology and ophthalmology, closely followed by those in gastroenterology, urology and neurology-neurosurgery. Only relatively few deal with tumor-specific reflection characteristics based on the study of large groups of patients.[1,10,13]

In order to assess the possibilities of ultrasonic diagnosis and differential diagnosis of space-occupying soft tissue lesions outside of the skull and orbit, we needed the most exact analysis possible of their reflection qualities. With this it is not only necessary to be able to determine the acoustic characteristics of the lesions themselves, but also of the border areas between tumor and surrounding tissue. The diagnosis of sonographic variants must also be considered, including, if possible, their pathologic-anatomic origins.

Among the tumors routinely examined by us, those in the kidney region comprise a large group. Of these, the nephroblastomas, with 5 histologically verified cases, are the most frequently seen in childhood. These have shown uniform sonographic characteristics, the description of which forms the basis of this report.

MATERIAL

The 5 patients with nephroblastoma were sent to us for examination from the University Childrens' Hospital as part of the routine preoperative investigation, which includes angiography in addition to other examinations. The ages ranged from $2\frac{10}{12}$ to $5\frac{5}{12}$ years with an average of $4\frac{0}{12}$ years. As is our usual therapy plan, all children received actinomycin D injections and irradiation preoperatively.

Since the diagnosis in all the patients could be made from history, clinical findings and roentgenologic examinations, the main purpose of the ultrasound examination was the exact, 3-dimensional representation of the actual size of the tumor for planning the therapy fields, as this cannot be calculated with sufficient accuracy from the angiograms alone.[2,12,14]

EXAMINATION TECHNIQUES

The basis of the ultrasound examination techniques will not be discussed here, as it has been previously reported by many authors, the last of whom was Olinger[11] in this JOURNAL.

Five points deserve special emphasis:

1. The examination technique itself is not different from that used for adults. However, in small children we use a transducer with a 1.5 cm. diameter crystal (frequency 2 MHz) instead of a 2 cm. diameter crystal, in order to obtain a better resolution perpendicular to the sound beam.
2. We use exclusively instruments with simultaneous A-scope/B-scan presentation (first that made by Kretz in Zipf, Austria, and later that made by Unirad in Denver, Colorado) which enable an exact alignment of the beam through the structure of interest, with visualization of the path through the B-scan on the persistence oscilloscope.
3. The A-scope examinations are always made without a threshold cut-off. Intensity and depth compensation are so adjusted that the echo signal which passes through the area of interest has maximal and equal amplitude both near the proximal and distal borders. An overcharge is to be avoided.
4. The image of the normal kidney or liver serves as the parameter for the proper adjustment of the instrument. This is

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considered correct when the parenchyma is visualized as a reflection-free zone with equally strong demonstration of the proximal and distal borders.

5. Transverse and longitudinal tomographic sections are always made through the tumor regions, as well as multiple A-scope pictures with the beam directed through the tumor and, when possible, also through the liver and/or kidney regions.

Figures 1, *A* and *B*, are ultrasound tomograms of a normal kidney: (*A*) a transverse section through both kidneys, done with the patient in the prone position, with demonstration of the small central reflections of the borders between the kidney parenchyma, renal pelvis and the hilus vessels; and (*B*) a longitudinal section through one kidney, also done with the patient in the prone position. Both pictures illustrate the standard adjustment, as described above, for the tomography apparatus.

The same standards are also used for ultrasound tomography of the liver. This organ is often involved by Wilms' tumors of the right kidney. For this reason, a normal transverse tomogram (at the level of the xiphoid) is shown in Figure 2.

REPORT OF CASES

CASE I. (280165 GN), a $5\frac{1}{2}$ year old boy with a left kidney tumor (Fig. 3, *A* and *B*). In the transverse tomogram, obtained with the patient in the prone position, the tumor is seen as a practically echo-free zone which extends toward the right to the level of the spine. The A-scope shows only very small reflections in the tomographically echo-free zone. (The sound beam direction is shown in all cases in the B-scan with a white line and is marked with an arrow.) It is not possible to differentiate between renal parenchyma and tumor.

CASE II. (030668 SK), a $3\frac{3}{12}$ year old boy with a tumor of the left kidney (Fig. 4, *A–C*). The tumor extends ventrally and caudally from the kidney region with the lowest part reaching the anterior abdominal wall. The transverse tomogram was obtained with the patient in the supine position, through the upper third of the tumor and includes part of the right lobe of the liver. The reflection characteristics of the tumor are identical with those of the first patient: there were practically no tumor echoes in the tomogram and only a few higher tumor echoes in the A-scope.

CASE III. (230368 BW). This is our youngest patient, a $2\frac{2}{12}$ year old girl, with a tumor of the right kidney (Fig. 5, *A–C*). The tumor extended anteriorly to the abdominal wall and on the left

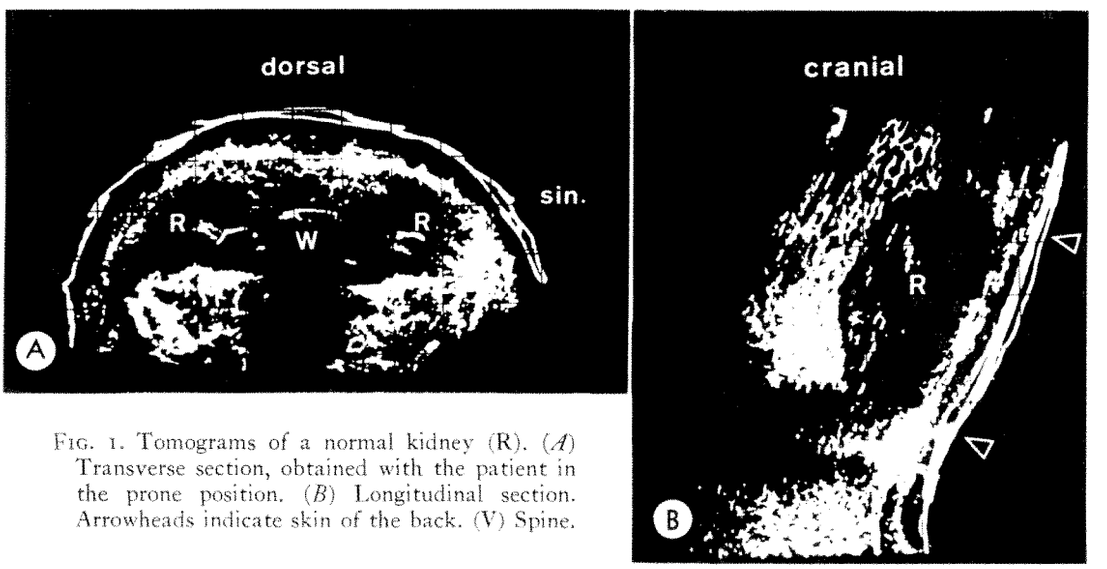


FIG. 1. Tomograms of a normal kidney (R). (*A*) Transverse section, obtained with the patient in the prone position. (*B*) Longitudinal section. Arrowheads indicate skin of the back. (V) Spine.

to in front of the spine. The liver is not clearly distinguishable from the tumor in either the transverse or the longitudinal B-scan. In the tumor itself there were numerous strong reflections both in the tomogram and in the A-scope. In the rest of the tumor tissue the A-scope showed only very weak echoes. At operation it was demonstrated that the tumor had grown together with the liver and that there were large liquefied areas of tumor necrosis.

Case IV. (010267 SD), a $4\frac{5}{12}$ year old girl with a right kidney tumor which extended to the spine (Fig. 6, *A–D*). In addition, the tumor had grown cranially and displaced the liver, so that the left border of the liver reached the left chest wall in the midaxillary line. The caudal portion of the tumor lay in the right lower abdomen. In the tumor, there were multiple reflections seen in both the B-scan and A-scope. The border between the tumor and the liver was not recognizable in either the transverse or the longitudinal tomogram. The tumor size, necrosis (seen as multiple strong reflections), and liver infiltration (seen as the lack of a definite border between liver and tumor), as diagnosed ultrasonically, were confirmed at surgery.

Case V. (121066 PV). This child, $5\frac{5}{12}$ years old, is our oldest patient (Fig. 7, *A–E*). The large tumor of the right kidney displaced the liver cranially and ventrally. The good demonstration of the borderline between tumor and

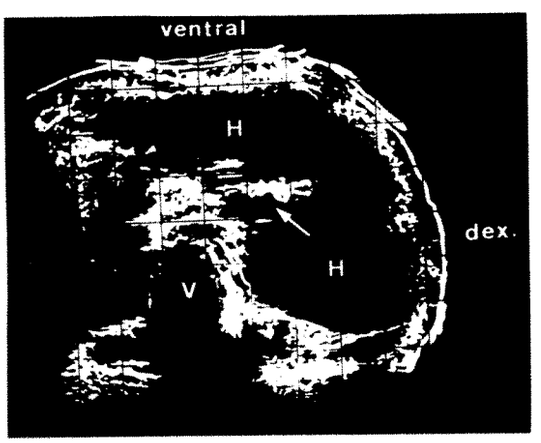


Fig. 2. Transverse tomogram of a normal liver (H). The arrow points to the hilus of the liver. (V) Spine.

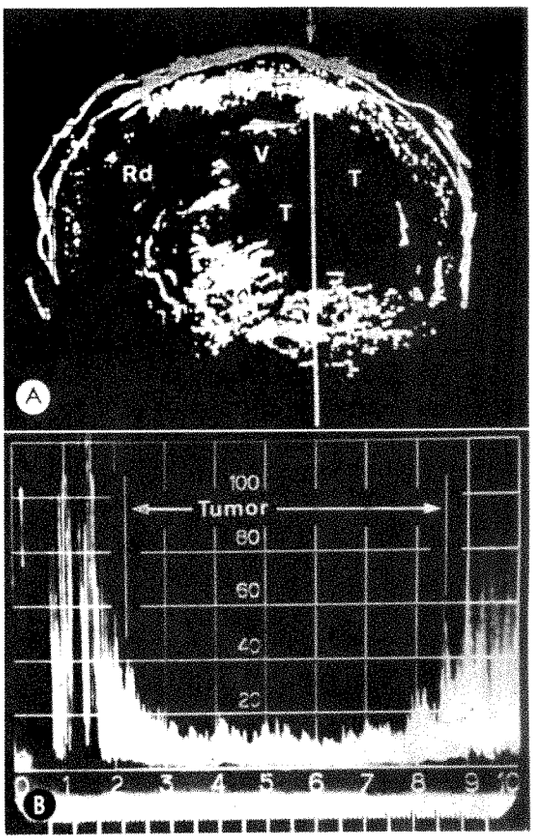


Fig. 3. Case I. (*A*) Transverse tomogram through the kidney region with the patient in the prone position. (T) Tumor of the left kidney; (Rd) Right kidney; (V) Spine. The location and direction of the ultrasonic beam through the B-scan, as seen on the A-scope (*B*), are shown by the arrow and the white line in *A*.

liver in the transverse and in the longitudinal B-scans speaks against an infiltration of the liver, at least in the pictured areas. In both the tomogram and the A-mode pictures there were, in general, only very weak sound reflections with only scattered "spike" echo signals registered within the tumor. The transverse B-scan at the level of the xiphoid is of particular interest: here, next to the typical reflection-free zone of the liver, is an abnormal round zone, about 6 cm. in diameter, with weak reflections located in front of the spine and a corresponding displacement of the liver ventrally and to the right. The ultrasonic diagnosis was confirmed at surgery: a large Wilms' tumor of the right kidney with isolated small areas of necrosis,

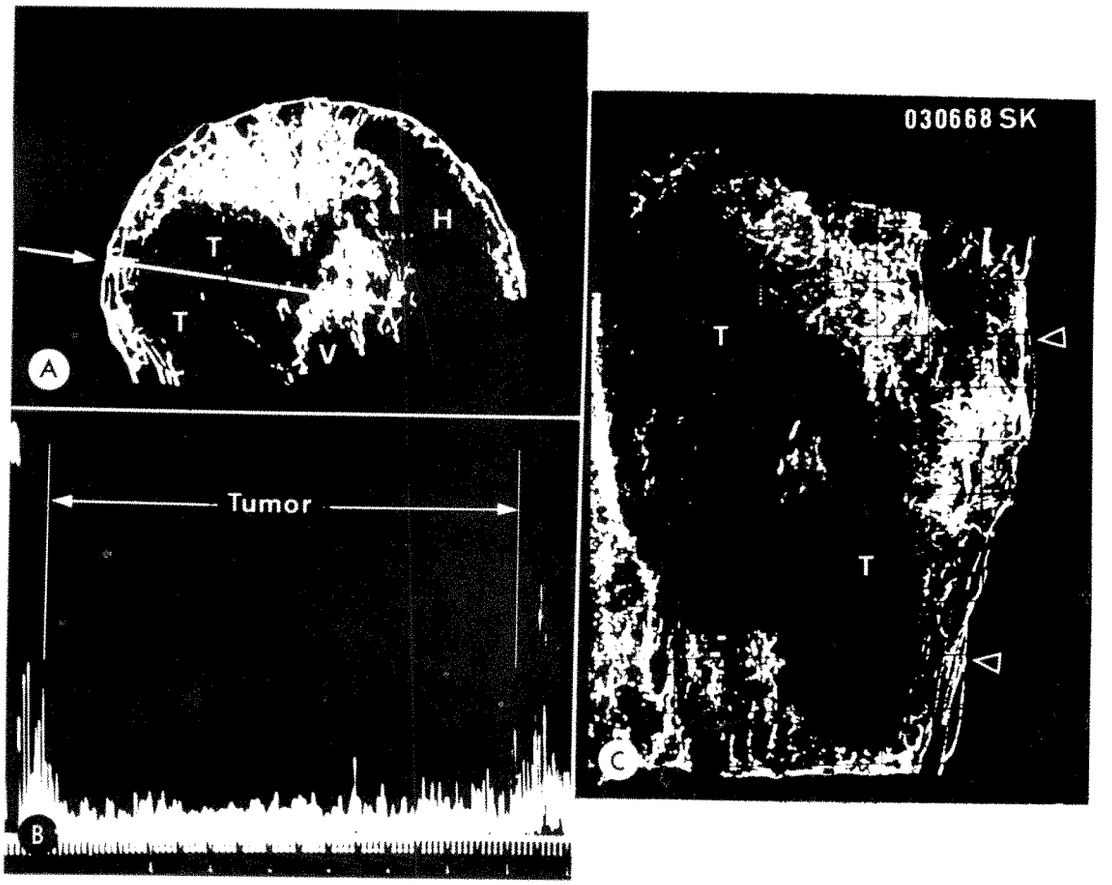


FIG. 4. Case 11. (*A*) Transverse tomogram through the upper abdomen, with the patient in the supine position. (T) Tumor; (H) Liver; (V) Spine. The arrow and the white line in *A* indicate the position of the ultrasonic beam through the B-scan, as seen on the A-scope (*B*). (*C*) Longitudinal tomogram through the tumor in the midclavicular line. (The scale used in *C* is twice that in *A*.) Arrowheads indicate skin of the abdominal wall.

displacement of the liver cranially and ventrally, and extension of a tumor plug prevertebrally-cranially without proof of liver infiltration.

DISCUSSION

All of the nephroblastoma patients examined by us had the following sonographic findings in common:

1. The tumor appeared in the B-scan as an extensive echo-free zone and was not distinguishable from the intact renal parenchyma. Scattered strong echoes within the tumor were probably caused by necrosis.
2. The differentiation of the tumor from surrounding tissues with stronger reflections was sharp.
3. By increasing the sensitivity of the apparatus, the previously seen echo-free zones were no longer seen as echo-free zones, but as echo-containing structures, so that it was no longer possible to differentiate the boundaries of the various tissues.
4. The nephroblastoma was seen in the A-scope as a large homogeneous area. The amplitude of the reflection was very low (*i.e.*, of low energy) and was not distinguishable from that of the normal kidney or liver. However, additional narrow, high echo spikes could be dem-

onstrated in the tumor when necrotic foci existed.

The impossibility of the exact delineation of the nephroblastoma from the kidney is caused by the infiltrating nature of the tumor growth. The infiltration obliterates the normal tissue structure, making it impossible to separate tumor from normal parenchyma by ultrasound. This same behavior also characterizes the relationship to the liver. Where the tumor is only in contact with the liver, there is a clear visualization of the liver and tumor capsules (Case v). Indeed, both surfaces are inseparable when there are no weaker reflecting structures between them. With tumor infiltration of the liver (Cases III and IV) the capsule is destroyed, and the invasion of the liver parenchyma by the tumor, which has the same acoustical properties, causes the sonographically seen boundary between the 2 different tissues to disappear. The differentiation between tumor and liver is, in this case, only possible through the presence of isolated "spike" reflections found only in the tumor tissue and never in the normal liver parenchyma (Cases III and IV).

The lack of patient risk and discomfort,

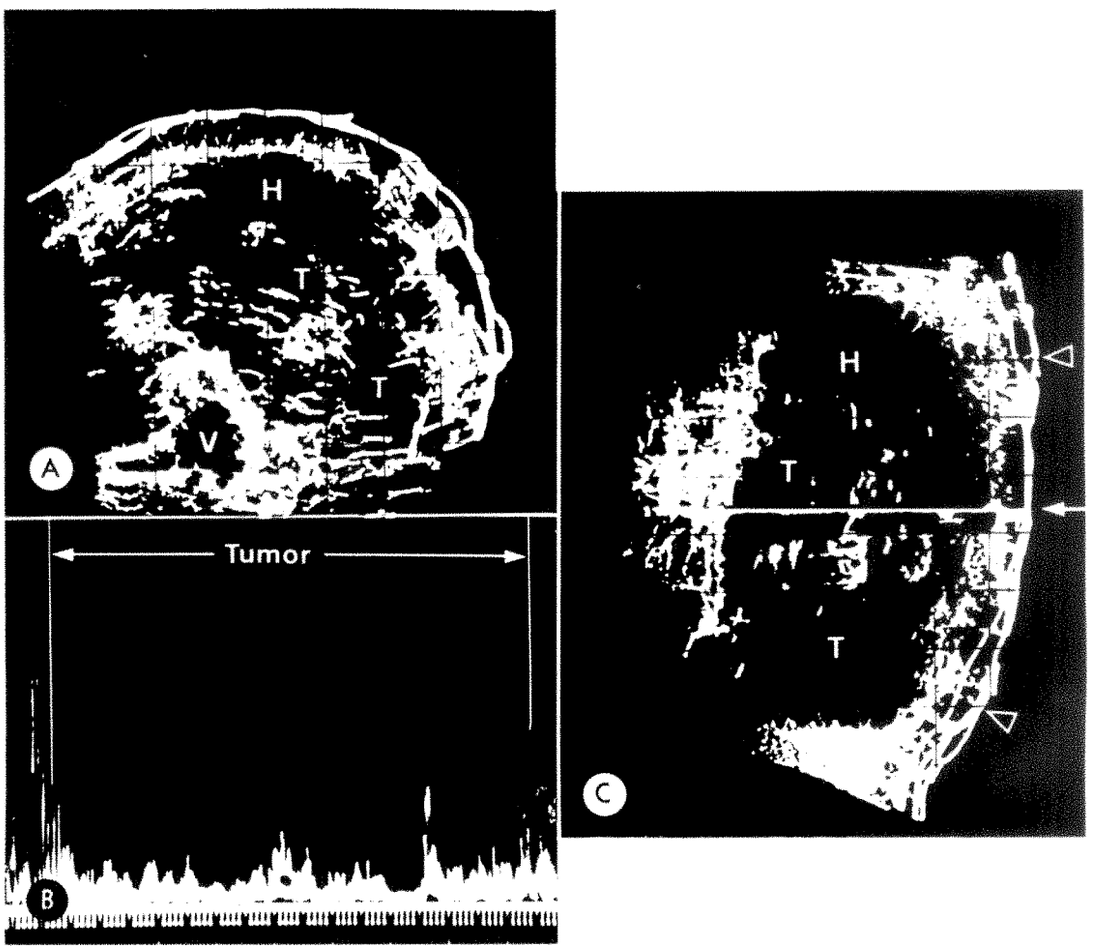


FIG. 5. Case III. Tumor of the right kidney. (*A*) Transverse tomogram taken at a level midway between the xiphoid and the umbilicus with the patient in the supine position. (*C*) Longitudinal section through the right midclavicular line. The tumor (T) is not clearly distinguishable from the liver (H). (V) Spine. Arrowheads indicate skin of the abdomen. (*B*) A-scope as shown in *C*.

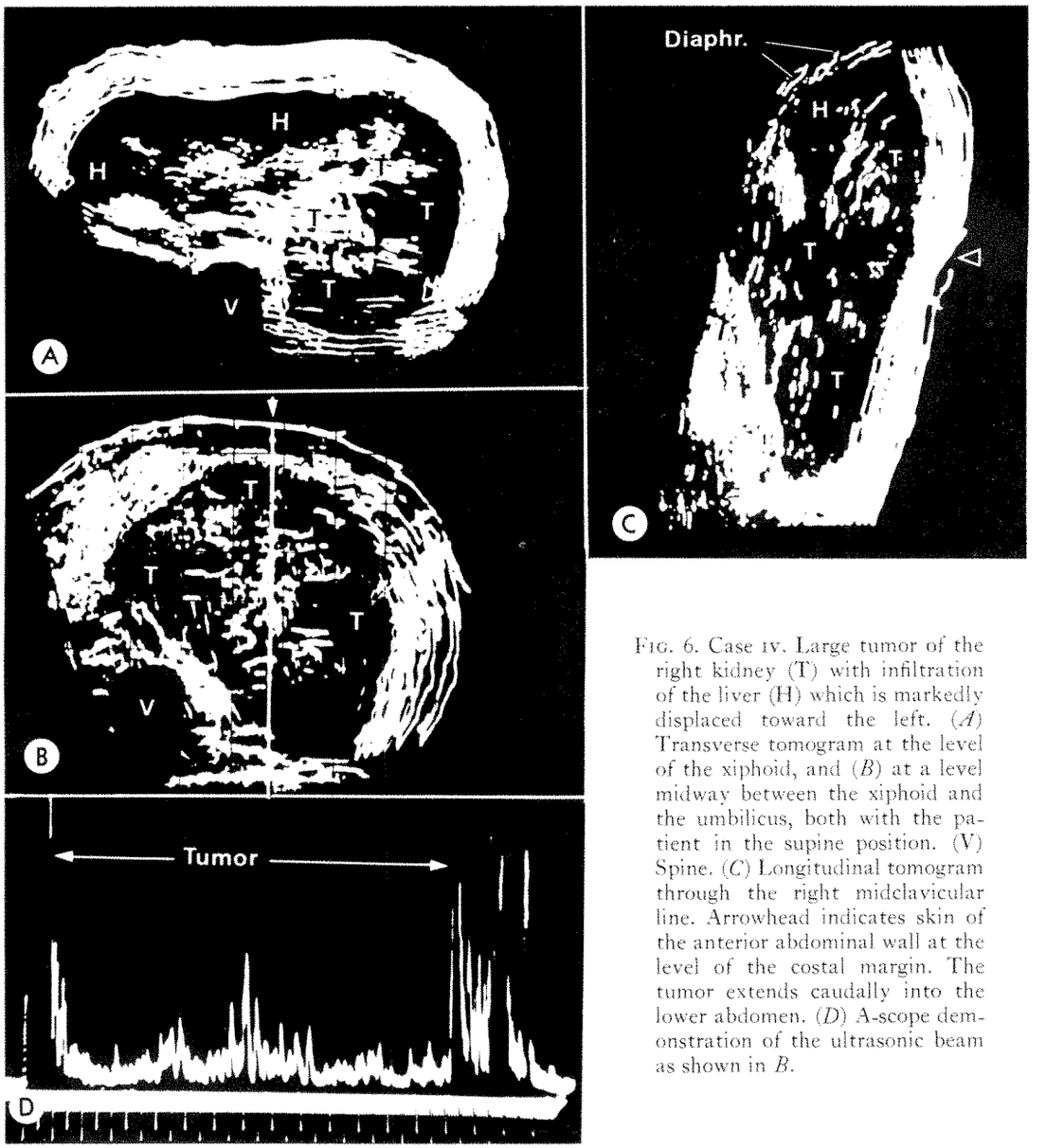


FIG. 6. Case IV. Large tumor of the right kidney (T) with infiltration of the liver (H) which is markedly displaced toward the left. (*A*) Transverse tomogram at the level of the xiphoid, and (*B*) at a level midway between the xiphoid and the umbilicus, both with the patient in the supine position. (V) Spine. (*C*) Longitudinal tomogram through the right midclavicular line. Arrowhead indicates skin of the anterior abdominal wall at the level of the costal margin. The tumor extends caudally into the lower abdomen. (*D*) A-scope demonstration of the ultrasonic beam as shown in *B*.

the 3-dimensional demonstration and the good visualization of the tumor and its relationship to the liver confirm the particular value of the ultrasonographic method described here in the diagnosis of nephroblastoma, as well as in following the therapeutic effect. The original results supplement the different roentgenologic examinations and enable an optimal radiation plan. In these children, the majority of whom were already severely weakened, the accurate, 3-dimensional measurements allowed the determination of the best radiation plan giving optimal tumor irradiation and maximal protection of the normal, healthy tissue.

Since the radiation therapy in nephroblastomas usually leads to an early impressive shrinking of the tumor mass, the later radiation dose can be adapted to the sono-

graphically seen tumor regression. This further protection of the healthy tissue from unnecessary radiation is possible only with the help of the ultrasonic tomography.

Hydronephrosis, polycystic kidneys, renal cysts, pararenal fluid collections (hematomas, abscesses), teratomas, neuroblastomas and sarcomas of differing types are to be kept in mind when considering space-occupying lesions in the kidney area in children. The value of ultrasonic tomography in the differential diagnosis of these space-occupying processes, particularly of the tumors, attains sufficient reliability only if there exist corresponding observations for comparison.

The following examples are cited:

Hydronephrosis. Independent of the re-

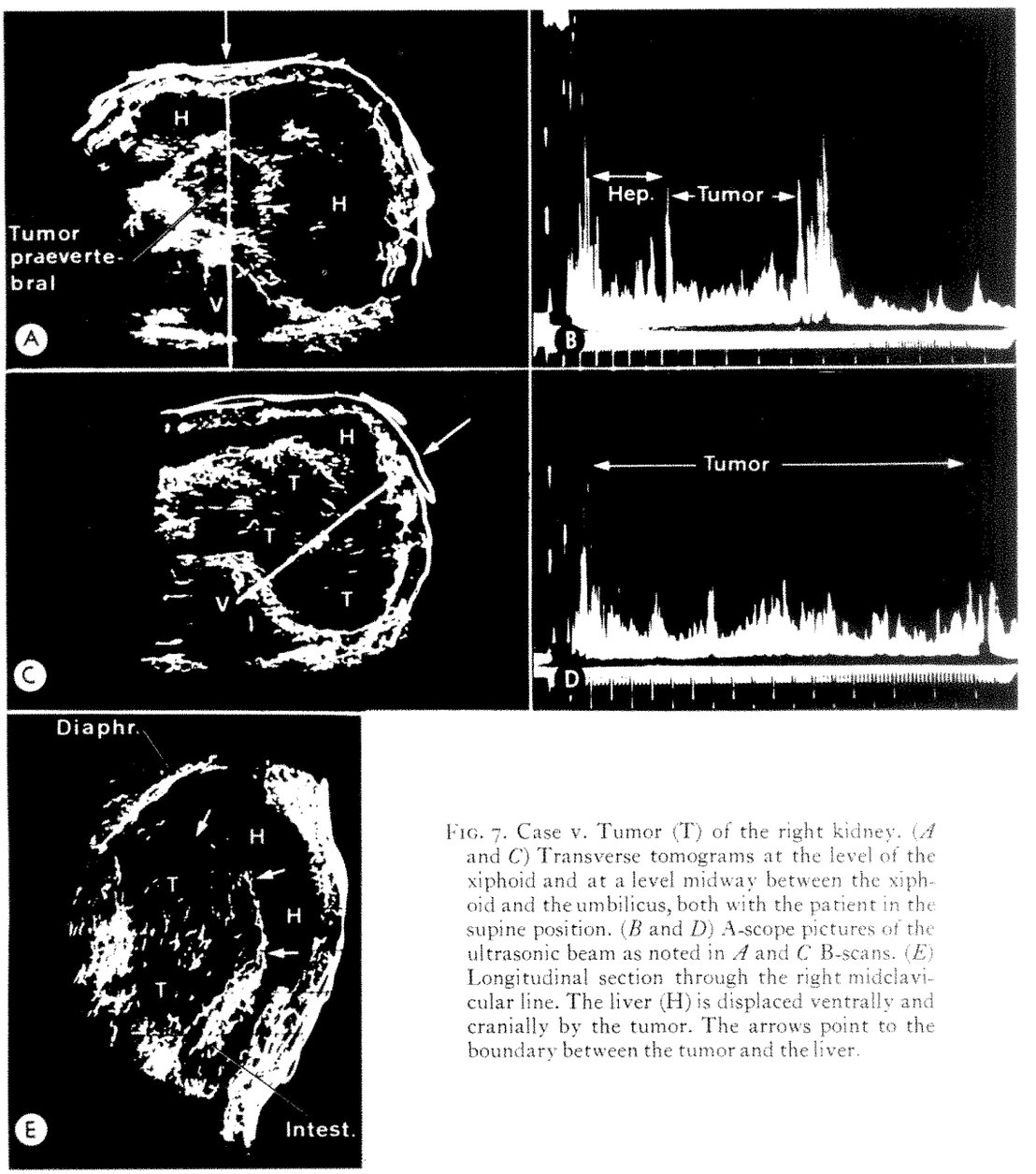


FIG. 7. Case v. Tumor (T) of the right kidney. (*A* and *C*) Transverse tomograms at the level of the xiphoid and at a level midway between the xiphoid and the umbilicus, both with the patient in the supine position. (*B* and *D*) A-scope pictures of the ultrasonic beam as noted in *A* and *C* B-scans. (*E*) Longitudinal section through the right midclavicular line. The liver (H) is displaced ventrally and cranially by the tumor. The arrows point to the boundary between the tumor and the liver.

sults of other examinations, particularly of the radiologic examination, the sonographic diagnosis of hydronephrosis can be presumed on the basis of an enlargement of the size of the kidney with reduction of the normal impedance differences between renal pelvis, hilus vessels and kidney parenchyma.[3,4] Whether or not the resulting diagnostic echo-free area can be seen in the A-scope, depends on the degree of widening of the pelvic and calyceal systems.

A *renal cyst* is seen as a more or less complete ring figure with nonreflecting contents. Analogous is the multilocular finding in polycystic kidneys. In both instances, the resulting expansion of the kidney can result in an enlargement of the renal space.[3–5]

A *pararenal fluid collection* leads to a reflection-free zone next to the weak reflections of the kidney. Thus, the adjacent areas are separable from one another by the demonstration of the renal capsule.[4]

In 1 patient whom we examined with a *teratoma* in the kidney region, only the tremendously large cyst, and not the solid part of the tumor, was recognized. This and the hypoplastic kidney were not sonographically distinguishable from the normal structures with strong reflections which surround the kidney.[7]

The *neuroblastoma*—as already known (1 reported case each by Kratochwil *et al.*,[9] Damascelli *et al.*,[3] and Hünig[7])—is seen as a strongly reflecting structure in all planes and depths of the tumor; *i.e.*, as a dense accumulation of reflections. In that the multiple fine calcifications are not the cause of these reflections, it could be that they originate from the fibrillary structures within the tumor tissue. Further examinations are needed to determine whether these reflection qualities are typical for all neurogenic tumors of this type or whether the acoustic behavior changes essentially with the degree of differentiation.

The same premise is also valid for *sarcomas*, the impedance differences of which are influenced by the histologic pattern. The tumor can be seen in the B-scan with the standard settings, either as a large echo-free zone (as with nephroblastoma), or as a massive accumulation of echoes (as with the neuroblastoma).[7,8]

By the description of the sound reflecting qualities of the neuroblastoma and their enumeration, pieces are added to the puzzle of differential diagnostic possibilities. For a detailed discussion, however, the comparison of our patients with those described in the literature is not sufficient. In the evaluation of the data presented here regarding the sonographic diagnosis and differential diagnosis of space-occupying lesions of the renal area, one must realize that the correlation of sonographic patterns to histologic diagnosis is often possible only with the help of other relevant data. This same situation exists in the evaluation of many other examination procedures.

SUMMARY

The ultrasound reflection characteristics in 5 patients with Wilms' tumors are described. In the A-scope, the amplitude of the tumor echoes is not distinguishable from that of the kidney and liver, so that the boundary between tumor and renal or, if infiltrated, hepatic parenchyma cannot be defined. Necrotic foci within the tumor are probably the cause of the isolated high energy reflections. In the B-scan the Wilms' tumor appears as a well defined, more (necrosis?) or less echo-free zone because of its very low impedance differences when the apparatus is optimally adjusted for the visualization of the kidney and liver. When the sensitivity is increased more than this, the weak echoes are amplified to the point where normal parenchyma and tumor tissue are no longer distinguishable from one another.

While the value of ultrasound tomography can be considered as proven for the optimal planning of radiation therapy, the additional information from the simultaneous A-scope examination could possibly lead to a classification of the various differential diagnostic possibilities based on

their internal structures. These further possibilities are implied here with the description of the known sound reflecting qualities of other space-occupying processes in the kidney region.

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THE IMPORTANCE OF SUBTRACTION IN THE ANGIOGRAPHIC EVALUATION OF EXTRA-ADRENAL PHEOCHROMOCYTOMAS*

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USE of the subtraction method has led to identification of 2 extra-adrenal pheochromocytomas which could not be seen on conventional aortograms.

We are presenting the findings to emphasize the importance of subtraction in patients with this disease.

REPORT OF CASES

CASE I. Ten years ago a 40 year old man had a 3 month history of episodic flushing, sweating, and pounding pain in the abdomen and the head. A retroperitoneal air study revealed a left suprarenal mass; at exploration a benign pheochromocytoma was found in the left adrenal gland. Following left adrenalectomy the patient was well until 5 days prior to admission when the exact symptomatology caused by the previous pheochromocytoma recurred. His blood pressure was 200/120 mm. Hg.

The admission physical examination was unremarkable except for a blood pressure of 170/120 mm. Hg. Urinary VMA levels ranged between 11.5 and 16.5 mg. for a 24 hour period (normal up to 10 mg.). Catecholamines and metanephrines were not done. A tentative diagnosis of pheochromocytoma was made and the patient was placed on 15 mg. of dibenzylene 3 times a day for 3 days prior to angiography.

Aortography (Fig. 1, *A* and *B*) revealed a 2.5×3.5 cm. area of tumor vessels and increased contrast medium accumulation in the region of the right adrenal gland. The angiographic diagnosis was pheochromocytoma. At exploration the tumor was excised and the diagnosis confirmed. In addition, a second 2.0 cm. in diameter tumor was found in a sympathetic ganglion separate from the right adrenal gland adjacent to the entrance of the right renal vein into the inferior vena cava. This was removed and also found to be a pheochromocytoma. Because the second pheochromocytoma could not be identified on the non-subtracted aortogram, even in retrospect, it was subtracted. This demonstrated a 2.0 cm. in diameter area of increased contrast medium accumulation overlying the right pedicle of the 2nd lumbar vertebral body (Fig. 1*C*).

CASE II. A 53 year old woman had a 2 year history of labile, poorly controlled hypertension (up to 200/116 mm. Hg). Six months prior to admission she had a hemiparesis and slight aphasia which cleared in a month. Two regitine tests were positive 1 month prior to admission.

On admission the blood pressure was 180/100 mm. Hg, but the physical examination was otherwise unremarkable. Urinary catecholamines were 818 and 410 μg. for 24 hours (normal up to 100 μg.); metanephrines were 5.8 and 2.0 mg. for 24 hours (normal up to 1.3 mg.) and VMAs were 7.1 and 5.1 mg. for 24 hours (normal up to 0.9 mg.). The patient was placed on dibenzylene (dosages ranging from 10 to 30 mg. every 8 hours for 9 days prior to angiography).

Aortography (Fig. 2, *A* and *B*) demonstrated mild irregularities in the right main renal artery, but no pheochromocytoma could be identified. Subtraction films demonstrated several tumor vessels and increased accumulation of contrast medium in a 2.0 cm. in diameter area superimposed on the right inferior 12th vertebral body (Fig. 2*C*).

At exploration the tumor was in a celiac ganglion medial to and separate from the right adrenal gland. The histologic diagnosis was pheochromocytoma.

DISCUSSION

The subtraction technique has been a standard part of neuroradiologic angiographic examinations for several years. The method has not been used widely in visceral angiography because of the changing gas

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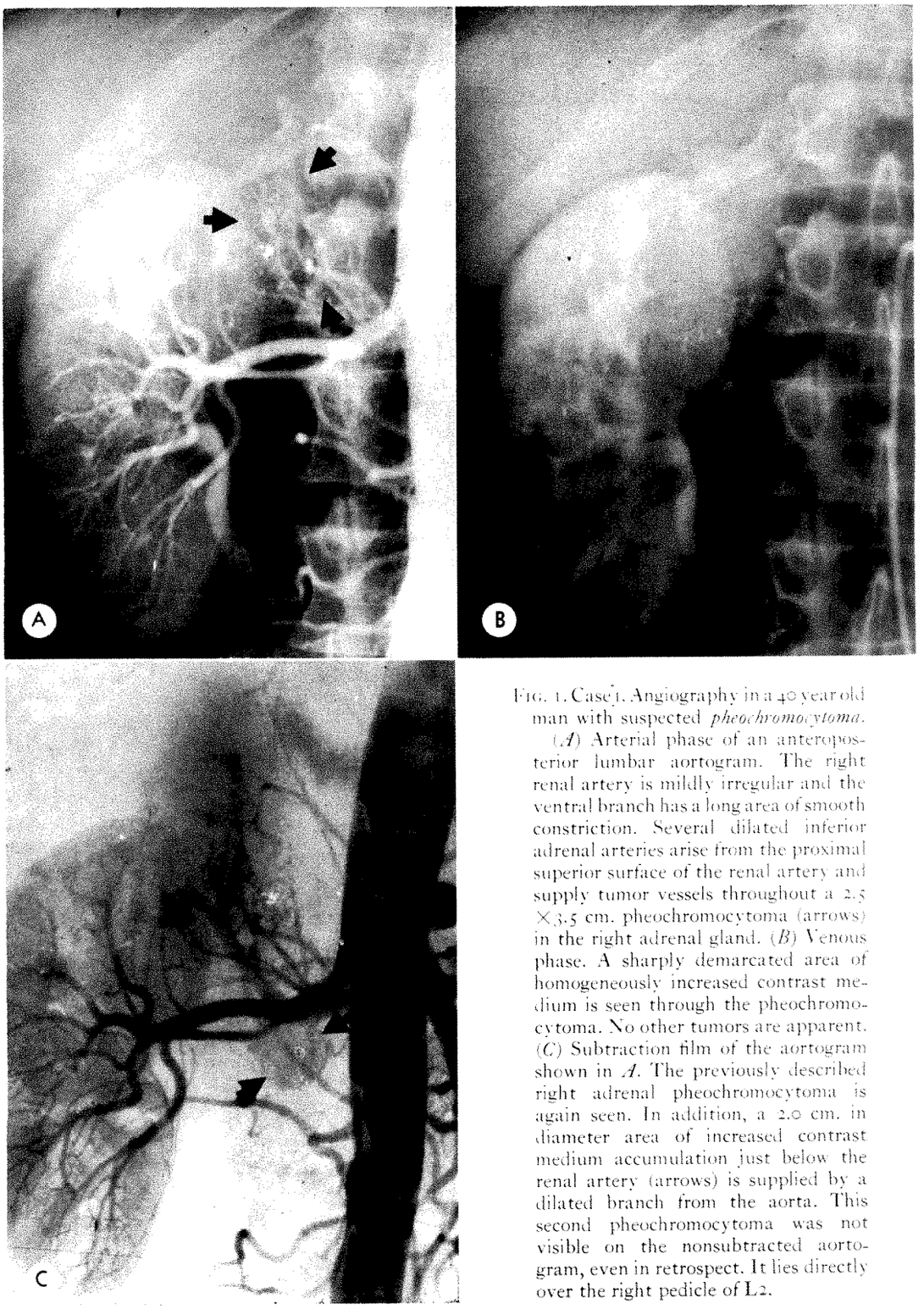


FIG. 1. Case 1. Angiography in a 40 year old man with suspected *pheochromocytoma*. (*A*) Arterial phase of an anteroposterior lumbar aortogram. The right renal artery is mildly irregular and the ventral branch has a long area of smooth constriction. Several dilated inferior adrenal arteries arise from the proximal superior surface of the renal artery and supply tumor vessels throughout a 2.5 × 3.5 cm. pheochromocytoma (arrows) in the right adrenal gland. (*B*) Venous phase. A sharply demarcated area of homogeneously increased contrast medium is seen through the pheochromocytoma. No other tumors are apparent. (*C*) Subtraction film of the aortogram shown in *A*. The previously described right adrenal pheochromocytoma is again seen. In addition, a 2.0 cm. in diameter area of increased contrast medium accumulation just below the renal artery (arrows) is supplied by a dilated branch from the aorta. This second pheochromocytoma was not visible on the nonsubtracted aortogram, even in retrospect. It lies directly over the right pedicle of L2.

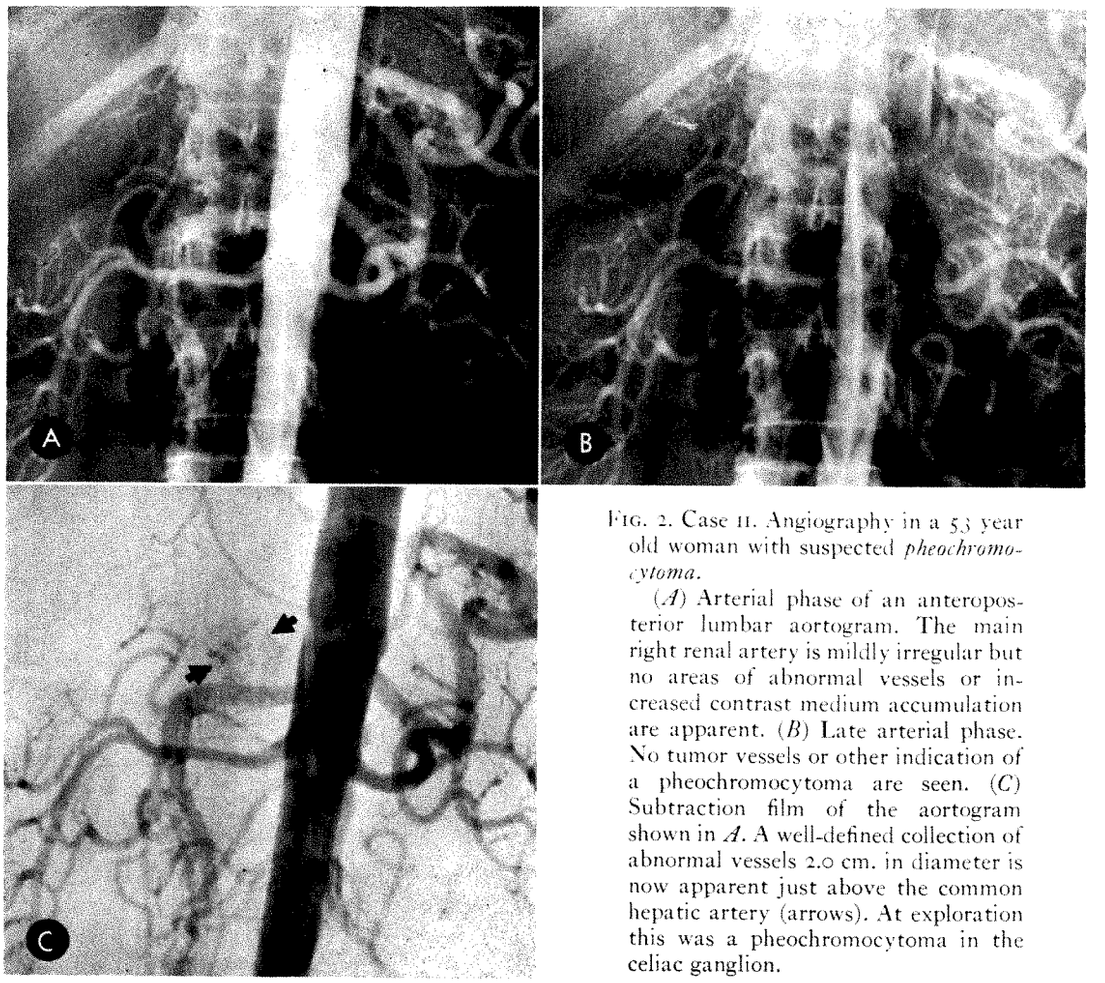


FIG. 2. Case 11. Angiography in a 53 year old woman with suspected *pheochromocytoma.*

(*A*) Arterial phase of an anteroposterior lumbar aortogram. The main right renal artery is mildly irregular but no areas of abnormal vessels or increased contrast medium accumulation are apparent. (*B*) Late arterial phase. No tumor vessels or other indication of a pheochromocytoma are seen. (*C*) Subtraction film of the aortogram shown in *A*. A well-defined collection of abnormal vessels 2.0 cm. in diameter is now apparent just above the common hepatic artery (arrows). At exploration this was a pheochromocytoma in the celiac ganglion.

patterns which occur during examinations. However, we have found the method helpful in the evaluation of retroperitoneal organs which overlie the spine, particularly the pancreas. With this method small pseudocysts and islet cell adenomas in the pancreas have been identified. Other authors advocating angiography for the diagnosis of pheochromocytoma have not mentioned subtraction.[3,5,10] Since the retrospective discovery of the extra-adrenal pheochromocytoma in Case 1, we have made subtraction a routine part of the evaluation of patients with suspected pheochromocytoma. The 2 patients reported are among 8 examined and among 4 in whom tumors were actually found. This high percentage of extra-adrenal pheochromocytomas probably reflects only the small number of patients. In large series 10 to 15 per cent of pheochromocytomas are extra-adrenal. The incidence is higher in children.[3,13] An increased incidence of pheochromocytomas occurs in neuroectodermal diseases, such as neurofibromatosis, Sturge-Weber's disease, tuberous sclerosis, and von Hippel-Lindau's disease.[11]

Extra-adrenal pheochromocytomas arise from the chromaffin cells of the paravertebral sympathetic ganglia from the cervical area through the pelvis. Cervical and thoracic pheochromocytomas are rare [2,6] most extra-adrenal tumors lie in the abdomen. A common site is adjacent to the renal pedicle, as in Case 1. Another site of predilection is the organ of Zuckerkandl.[7] Very

rarely they are found in the bladder or along the ureter.[1] The sympathetic ganglia frequently are superimposed on the vertebral column in anteroposterior aortograms and the use of subtraction technique should, therefore, increase the preoperative diagnosis of the extra-adrenal tumors.

About 5 per cent of pheochromocytomas are multiple. Multiple tumors occur more frequently in children.[12] Rarely, the second tumor is in the opposite adrenal gland, but second tumors are usually extra-adrenal. Even though 1 tumor is well demonstrated by aortography, as in Case 1, therefore, a careful search must be made for a second lesion and subtraction will aid in this search.

An interesting aspect of the first patient was the successive nature of the pheochromocytomas. A similar case was reported by Pyle.[9] His patient was a child and there was a much shorter period between the recurrence of the tumors in right and left glands. It is also interesting that the diagnosis of the second tumor was made by the patient himself because of the similarity of the symptomatology to the previous pheochromocytoma.

The narrowing of the main renal artery branch in both patients has been observed in other patients with pheochromocytoma.[10] Although no proof is available, this finding may be related to the pressor hormones secreted by the tumor. One of the authors (S.R.R.) has seen a patient with a pheochromocytoma in whom arterial narrowing was present on a preoperative examination, while the artery appeared normal on an examination performed some months after the removal of the tumor.

SUMMARY

Two cases of extra-adrenal pheochromocytomas are reported, in which the subtraction of conventional aortograms played an important role in identification of the tumors.

The diagnostic value of the subtraction method in patients with this disease is emphasized.

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TUMORS OF THE URETER

PROBLEMS IN DIAGNOSIS

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PRIMARY carcinoma of the ureter, once considered rare, makes up about 1 per cent of all neoplasms of the upper urinary tract.[6] To date there have been about 1,200 tumors of the ureter reported in the literature.[14]

The purpose of this paper is to present our experience with tumors of the ureter and the problems encountered in their diagnosis.

PATHOLOGY

Benign tumors of the ureter are rare. Of the malignant neoplasms, those of transitional cell origin make up 75–85 per cent;[7,14] the remainder include squamous cell carcinomas, adenocarcinomas, and sarcomas. The term "papillary" refers not only to the gross villous frondlike projections characteristic of the tumor type, but is also used to describe the microscopic appearance. While some Grade 1 papillomas have been described as "benign," most authorities treat this lesion as potentially malignant. These tumors may demonstrate a multicentric origin with concomitant lesions being found in the renal pelvis and/or bladder, as well as multiple ureteral sites.[10,12] Bilateral ureteral tumors are rare, and simultaneous bilateral ureteral tumors extremely rare.[2,18]

A working classification presented by McDonald and Priestly[12] includes:

A. Papillary carcinoma Grade 1, 2, and 3
B. Papillary and infiltrating carcinoma Grade 2, 3, and 4
C. Nonpapillary infiltrating carcinoma Grade 2, 3, and 4.

Over-all evaluation then includes: the structure type (papillary or nonpapillary); the cell type (transitional or squamous); the degree of anaplasia (Broder's classification); as well as absence or presence of local infiltration and regional or distant metastases.

ETIOLOGY

The etiology of transitional cell carcinoma of the urinary tract, like that of other malignancies, is by no means settled. However, there is significant evidence that there are several chemical agents which may cause these tumors. There is good reason to believe that the metabolites of the parent aromatic amines, 2-naphthylamine, and 4-amino-diphenyl are carcinogenic in the urinary tract. There is also evidence to incriminate cigarette smoking as a cause. The mechanism is probably by way of enzymatic disturbances of tryptophan metabolism. Chronic infection and stone disease have also been implicated.[11]

CLINICAL AND UROLOGIC FINDINGS

Ureteral carcinoma is more common in men than women (3:1)[6] and is usually seen in patients over 50. The lower one-third of the ureter is the most frequent location.[1,17] Hematuria is usually the chief complaint, although flank pain does occur when there are obstructive manifestations. Given the patient in whom the clinical and roentgenologic findings are suspicious of pathology, cystoscopy with retrograde pyelography has been the most fruitful examination. Cystoscopy may disclose a concomitant bladder tumor or ureteral tumor protruding from an orifice. Simple biopsy of these lesions may be diagnostic.

Attempt at ureteral catheterization is the subsequent examination performed, and if the operator is fortunate enough to be able to traverse the obstruction, invaluable information may be gained. Two signs have

been considered diagnostic of tumor: (a) the Chevassu-Mock sign—increased ureteral bleeding following manipulation at the site of the tumor; and (b) Marion's sign—drainage of clear or clearing urine after passage of the ureteral catheter above or beyond the tumor.[1,9] Once the catheter has passed into the renal pelvis, collection of urine for culture and cytology, followed by routine pyelography with appropriate films, is accomplished. After this, some authorities have suggested the passage of a stone basket in an attempt to secure biopsy material. In those patients in whom the catheter cannot be negotiated past the site of obstruction, the coiling of the catheter below the obstruction may demonstrate the characteristic "sign" described by Bergman *et al.*[4] Ureteropyelography done by means of the "occluding tip" technique with the patient in a Trendelenburg position may give additional information. The use of the newly developed ureteroscope as well as the "brush technique" with cytology may facilitate diagnosis.



FIG. 1. Occluding tip pyelogram shows an obvious large filling defect in the distal right ureter which on histologic examination proved to be a Grade 2 papillary transitional cell carcinoma. The intravenous pyelogram demonstrated a right hydronephrosis and hydroureter with poor delineation of the tumor.

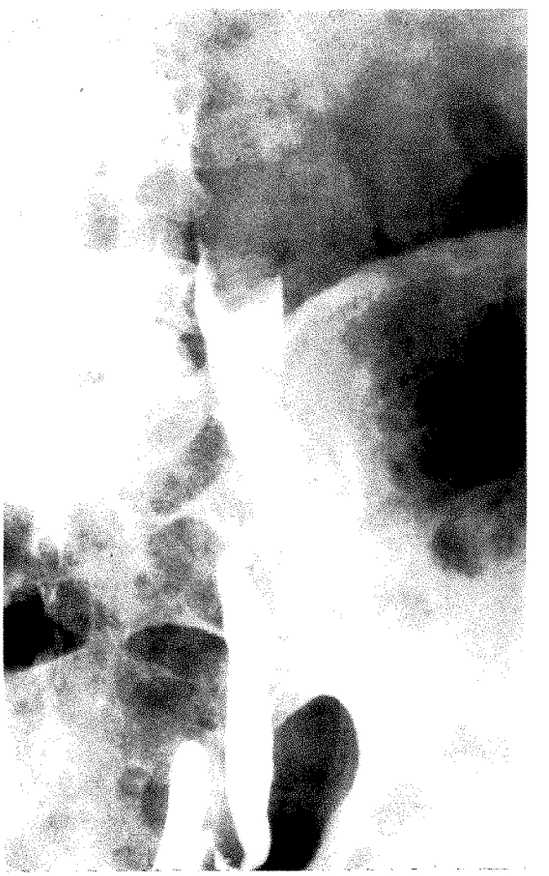


FIG. 2. Left retrograde pyelogram demonstrating the "goblet sign." This is due to the contrast material extending around the edge of the tumor and dilatation of the ureter. Note dilatation of the ureter below the tumor. Histologic examination showed Grade 1 papillary transitional cell carcinoma.

ROENTGEN DIAGNOSIS

Accurate diagnosis of these tumors is difficult and probably the least precise of any urologic lesion.[7] Filling defects in the ureter are frequently difficult or impossible to demonstrate on intravenous pyelogra-

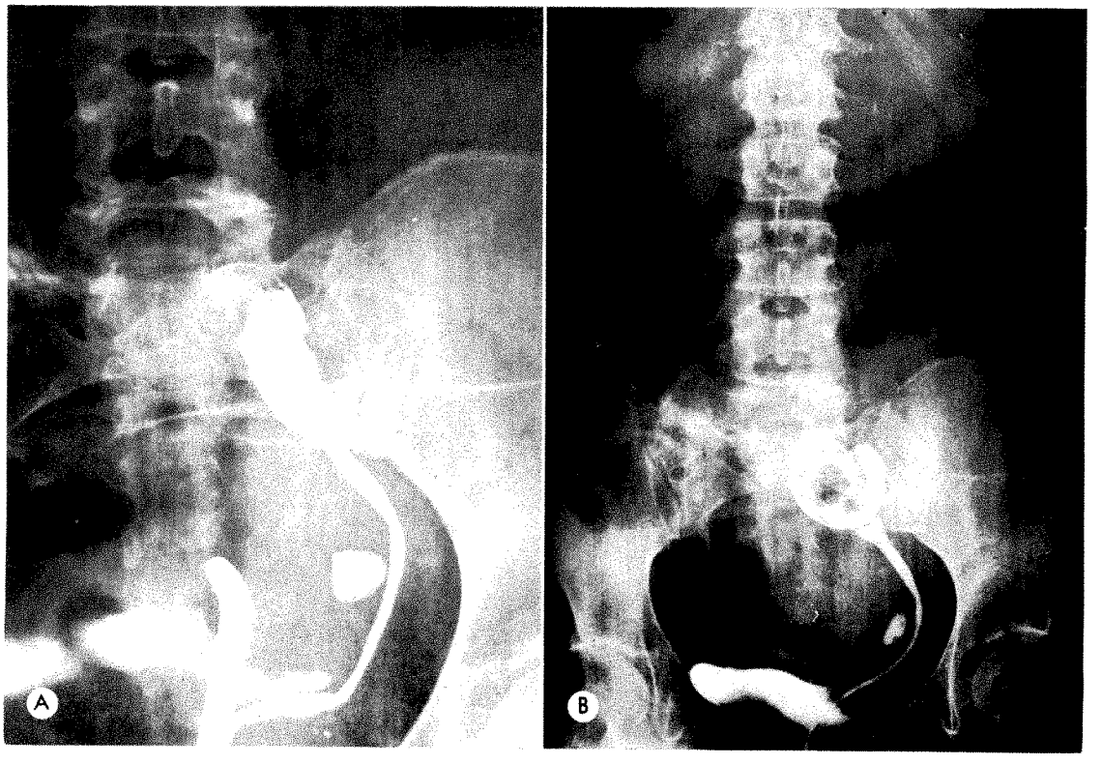


FIG. 3. Bergman's sign(s). (*A*) Left occluding tip pyelogram demonstrating a complete obstruction due to a large tumor. Note marked dilatation of the ureter below the tumor. (*B*) Left retrograde pyelogram demonstrating coiling of the catheter below and around the tumor. Histologic examination revealed Grade 2 papillary transitional cell carcinoma.

phy. This may be due to a nonfunctioning kidney, incomplete filling of the ureter, or failure of the ureter to dilate proximal to the tumor. There is a nonfunctioning kidney on the intravenous pyelogram in close to 50 per cent of the reported series.[3,6,14]

The occluding tip pyelogram is still probably the best method of demonstrating filling defects in the ureter (Fig. 1). One sign frequently mentioned in the literature is the goblet-shaped halo of opaque medium around the neoplasm (Fig. 2). When this is seen on an intravenous pyelogram, the deformity is reversed (the opaque medium is going over the top of the tumor), and it is referred to as an "inverted goblet" sign.[14]

In 1961, Bergman *et al.*[4] observed that the ureter is dilated immediately below a neoplasm in contradistinction to a mechanical obstruction from a stone where the ureter is collapsed below the stone (Fig. 3*A*). These authors also call attention to the frequency with which the ureteral catheter tends to coil in the dilated area below the tumor. This occurred in approximately half of their 7 cases and in 1 out of 6 in our own personal experience (Fig. 3*B*). Emmett and Witten[7] have referred to this characteristic coiling of the catheter as Bergman's sign.[7]

DIFFERENTIAL DIAGNOSIS

Small defects in the ureter are extremely difficult to evaluate (Fig. 4, *A–C*). A tumor should be suspected in *A* because of slight dilatation of the ureter below the filling defect. In *C*, there is also slight dilatation of the ureter below the defect, but this patient had a stone. Larger filling defects that cause a slight bulge in the contour of the

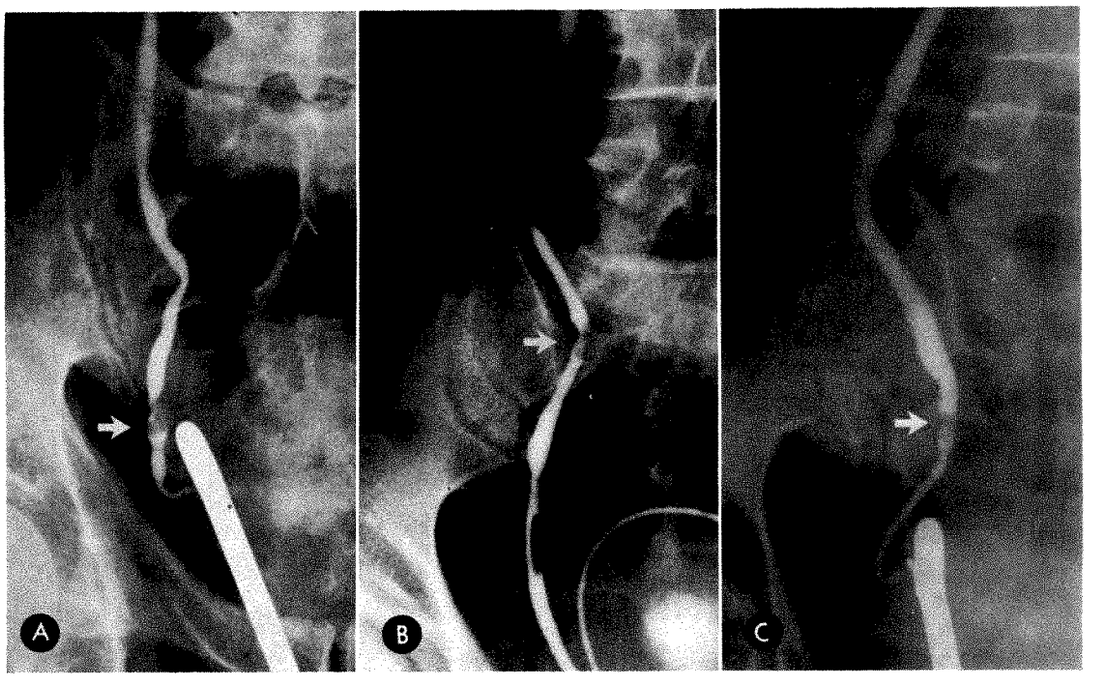


Fig. 4. Three small filling defects in the distal right ureter with similar appearance. (*A*) Defect (arrow) due to Grade 2 papillary transitional cell carcinoma. Note slight dilatation of the ureter below the filling defect. (*B*) Defect (arrow) due to nonopaque stone. (*C*) Defect (arrow) due to stone. There is a suggestion of slight dilatation of the ureter below the filling defect.

ureter are not as difficult to differentiate from nonopaque calculi, although the task is still not an easy one (Fig. 5, *A* and *B*).

Pyelitis and ureteritis cystica (Fig. 6) in most cases should not cause difficulty in diagnosis from tumor. The lesions are multiple and usually involve the upper third of the ureter. These defects are more apt to be confused with blood clots or nonopaque stones. However, their fixed position, relative uniformity in size, and characteristic notching in the contour of the ureter all help to differentiate these lesions.[13]

Solid nonpapillary infiltrating tumors of the ureter present an even more formidable diagnostic problem. The lesion may suggest a benign stricture or retroperitoneal fibrosis, but any obstructing lesion of this type, particularly in a male over 40 years of age, should be looked upon with suspicion (Fig. 7). To go a step further, Figure 8, *A* and *B* shows an almost identical appearance; yet in 8*A* we have a primary tumor and in 8*B* we are dealing with a secondary tumor.

Rarely, benign tumors have to be considered. Endometriosis can cause filling defects similar to papillary tumor and/or result in strictures similar to nonpapillary infiltrating tumor.[5] Benign strictures, periureteral fibrosis, varicosities, secondary carcinoma (direct extension or metastatic) and rarely malacoplakia[16] have to be differentiated from a primary nonpapillary infiltrating ureteral tumor.

TREATMENT

Treatment of these tumors is based on the patient's general condition and the status of both upper urinary tracts. No papillary tumor of the upper urinary tract should be treated until both kidneys and ureters have been completely and adequately visualized roentgenographically[7]

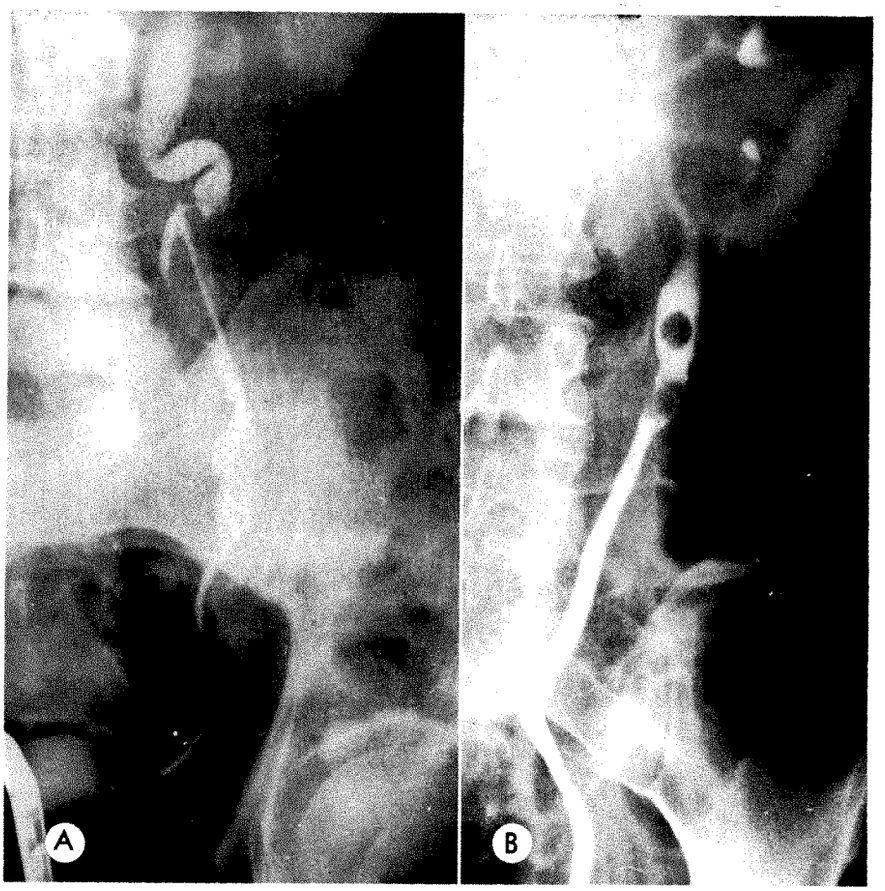


FIG. 5. (*A*) Large oval filling defect due to Grade 2 papillary transitional cell carcinoma. Note slight bulge in contour of the ureter at the tumor site, but no dilatation of the ureter below the tumor. (*B*) Two defects (one round and one oval) due to nonopaque calculi. Note slight dilatation of the ureter about both defects.

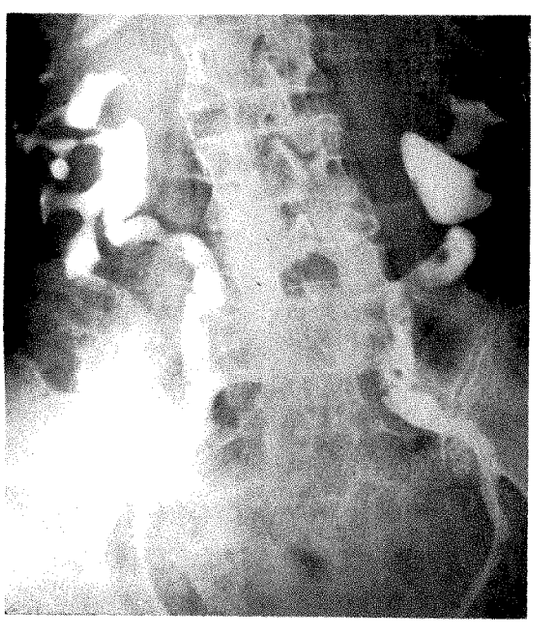


FIG. 6. Multiple small relatively uniform filling defects secondary to ureteritis cystica.

and the patient cystoscoped. For unilateral growths with a normal contralateral side, a nephroureterectomy with excision of a cuff of bladder has found the most favor among authorities.[8] Where this cannot be logically accomplished, a local excision with primary anastomosis or excision with urinary diversion has been employed. Survival rates depend on the tumor cell type, grade, stage, and extent of the disease.

SUMMARY

The various manifestations of carcinoma of the ureter are presented including the

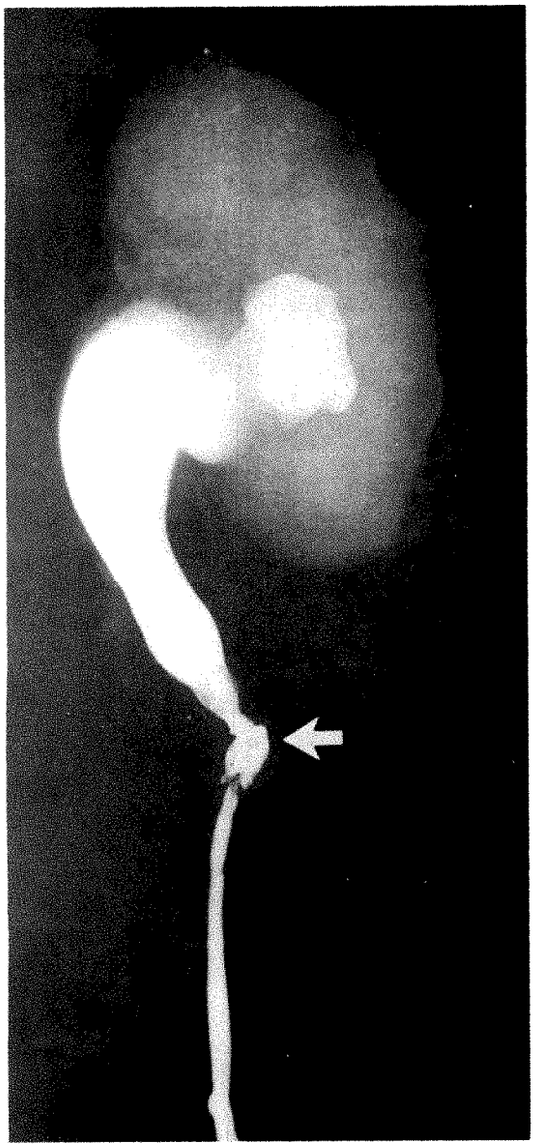


Fig. 7. Roentgenogram of contrast material filled operative specimen (nephroureterectomy) showing ureteral stricture at first believed to represent a benign process. On opening the specimen, the pathologist thought that the stricture was due to carcinoma. Microscopically, the stricture was benign, there being no evidence of neoplasm. The filling defect (arrow) just proximal to the stricture represents a nonopaque stone.

etiologic, pathologic, clinical, urographic, and roentgen findings.

Many entities have to be considered in the differential diagnosis, although nonopaque calculi appear to be the most common.

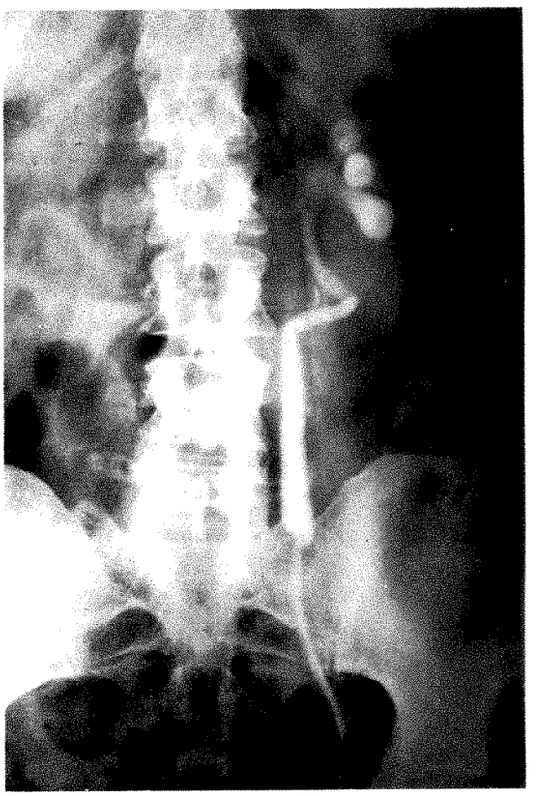


Fig. 8. Secondary ureteral involvement from extension of a primary carcinoma of the sigmoid.

The management of this disease is briefly discussed.

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DIAGNOSTIC ULTRASOUND SCANNING: A VALUABLE AID IN RADIATION THERAPY PLANNING*

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DIAGNOSTIC ultrasound scanning provides a rapid, accurate and reproducible method for obtaining body outlines, anatomic cross-sections of tumors and surrounding normal tissues and tissue thickness.

This article is concerned with the application of this technique to the problem of radiation therapy planning. The body contours and anatomic cross-sections can be optically enlarged to life size to establish field size and beam angles. This information can be computerized for radiation treatment planning.

Repeat ultrasound scanning provides a good method to follow the regression of deep-seated soft tissue tumors during and after completion of radiation therapy.

METHOD

A commercially available manual contact ultrasound "B" scanner was used in our studies.* A 2 MHz slightly collimated transducer was employed. Images were recorded on a storage type oscilloscope and then photographed with the attached camera. Multiple horizontal and longitudinal cross-sections were obtained of the proposed treatment area, usually at 2 cm. intervals. In some cases the proposed treatment fields had been set up by palpation, roentgenographic estimation, and general knowledge of the area to be treated. In other cases the ultrasound scans were done first, with delineation of the treatment fields. The borders of the treatment field were marked on the ultrasound pictures by making vertical lines from the skin surface with the transducer main bang (Fig. 1*B*).

* Picker Model 102.

In some cases the intensity of the base line was increased to exceed the storage level of the oscilloscope, making a line along the course of the ultrasound beam through the entire cross-section (Fig. 4*B*).

Initially we felt that we should have a full 360° outline and cross-section of the patient. To obtain this we suspended the patient between 2 treatment carts. If the patient's dimension was greater than 30 cm. in diameter, we would take ultrasonograms of the right and left halves of the area and then tape the 2 halves together. We now believe that a truer representation of the anatomy for treatment may be obtained by placing the patient in the treatment position for each portal and making as nearly a complete circumferential outline and scan as possible in that position. This varies from 180° to 270° with our equipment.

The body outline is first produced with the gain of the equipment turned down so that only the dot representing the transducer is recorded on the storage oscilloscope. While this outline is being produced, extreme care is taken, so that the transducer follows the surface of the body without causing it to be deformed by the pressure of the transducer. This outline is then photographed. Without erasing the outline from the storage oscilloscope, the gain is then increased, so that a good fill-in of the internal structures is recorded and photographed. The outlines and anatomic cross-sections are made on the 3 cm. scale for the trunk. The cervical area is recorded on the 2 cm. scale.

The outline and cross-section ultrasonograms are magnified to life size for use in treatment planning. This is accomplished

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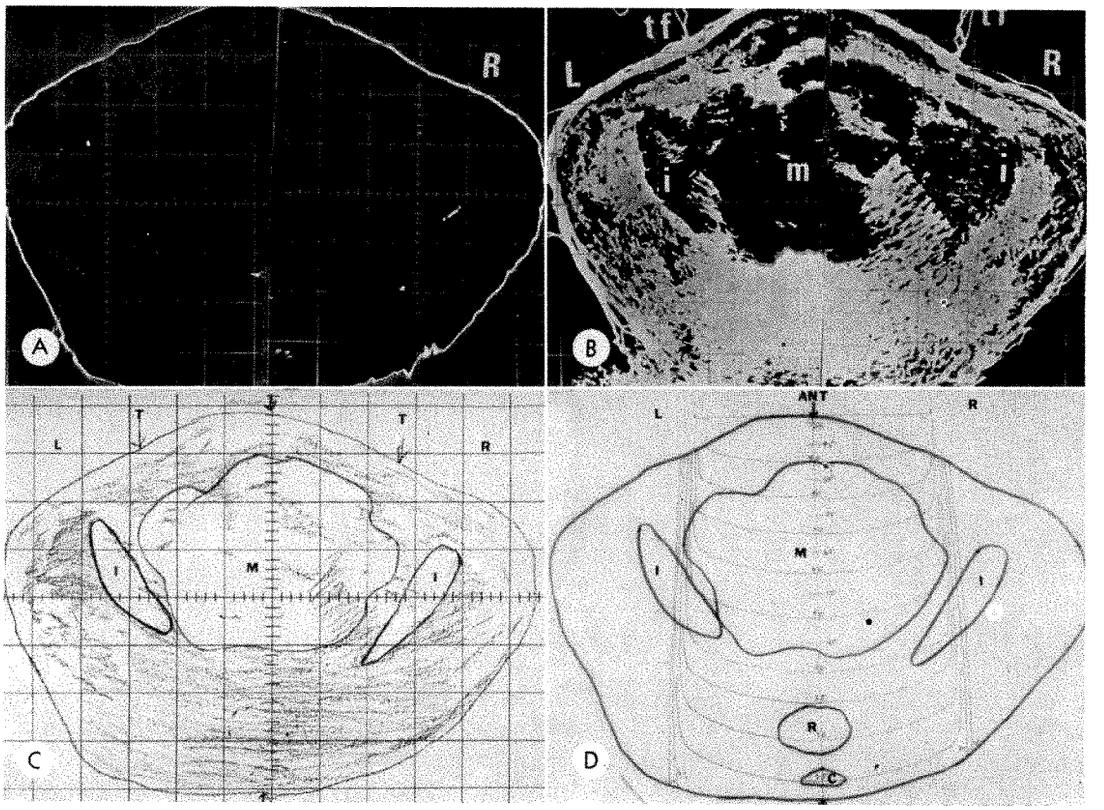


FIG. 1. Case 1. *Poorly differentiated sarcoma of the bladder.*

(*A*) Body outline at the midplane of the treatment field with patient's right on the right of the picture. The scale is 3 cm. per large division. (*B*) Filled in body cross-section at the same level. The mass of the tumor (m) is seen to fill the bony pelvis between the iliac wings (i). The lateral borders of the anterior treatment field are marked (tf) using the transducer main bang. (*C*) Cross-section of midplane of treatment field transferred by opaque projector to life size on 3 cm.×3 cm. grid paper. (*D*) The life size line drawing of the cross-section is transferred to tracing paper and the isodose curves from our cobalt 60 unit for this field size are drawn onto this line drawing for the anterior treatment port. The rectum (R) and coccyx (C) are also indicated. The same is done for the posterior treatment port, and the resulting isodose curves for the combined anteroposterior and posteroanterior treatment fields are obtained.

by projecting the photographic prints with a commercially available opaque projector† onto a piece of drawing paper which has been fastened onto the wall. This paper has a 3×3 cm. grid pre-drawn on it if we have used a 3 cm. scale, and a 2×2 cm. grid pre-drawn on it if we have used the 2 cm. scale. The grid lines on the projected print are superimposed on the grid lines on the paper by adjusting the position of the projector. When the grid lines across the entire projected print match the grid lines on the paper, we have a projected image of life size without significant distortion. The body outline, the important anatomic structure outlines and the tumor outlines are traced onto the paper from this projected image. This life sized drawing can then be used to plot isodose curves manually or to provide information to a computer for a print out of isodose information.

† Beseler Vu-Lyti III Opaque Projector.

REPORT OF CASES

CASE 1. M.W., a 71 year old white female, presented with frequency, nocturia and hematuria for 5–6 weeks' duration. Cystoscopy

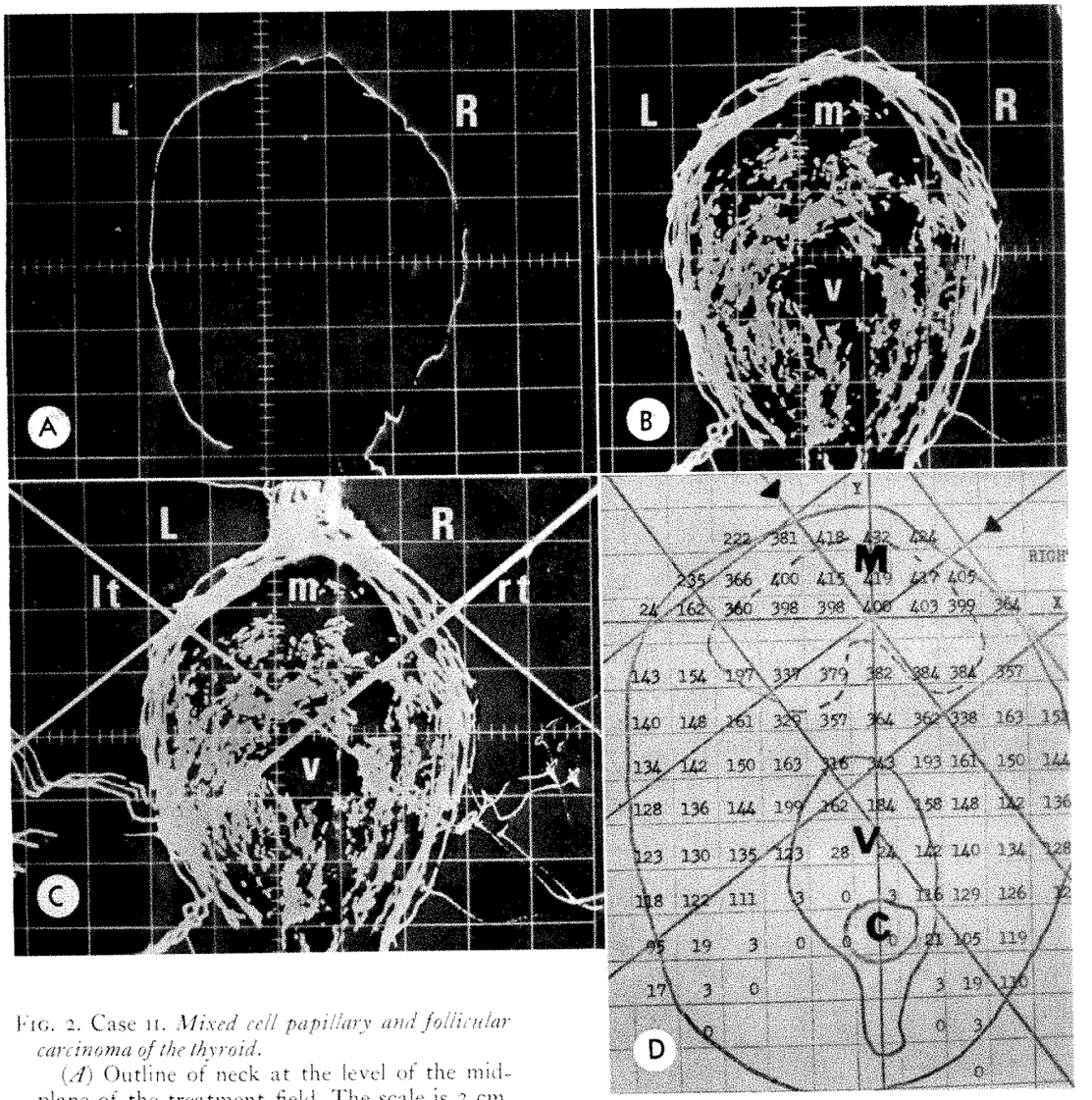


FIG. 2. Case 11. *Mixed cell papillary and follicular carcinoma of the thyroid.*

(*A*) Outline of neck at the level of the midplane of the treatment field. The scale is 2 cm. per division. (*B*) Filled in cross-section showing tumor (m) and vertebral body (v). (*C*) Proposed right treatment field (rt) and left treatment field (lt) superimposed on cross-section by increasing the intensity of the oscilloscope base line. (*D*) Then *C* is projected with an opaque projector onto a 1 cm. × 1 cm. grid paper and a line drawing of the outline of the tumor (M), vertebral body (V), spinal canal (C) and the treatment fields are drawn in. The numbers in the 1 cm. squares represent the dose in that square centimeter from a 200 rad dose to the zero point on the X and Y axis from a combined right to left treatment field. These are obtained from a computer. Note: the high dose is in the tumor area and the spinal cord dose is near zero.

showed a large papillary lesion around the bladder neck. A transurethral resection was attempted, but the tumor was too extensive. Six days later a partial cystectomy and reimplantation of the left ureter were done. At surgery it was felt that the tumor had been completely excised. The pathologic diagnosis was poorly differentiated sarcoma of the bladder, probably rhabdomyosarcoma. Two weeks later the patient had a palpable suprapubic mass and cystography showed an irregular mass within the bladder.

Ultrasound "B" scans showed an irregular soft tissue mass filling the bony pelvis and dis-

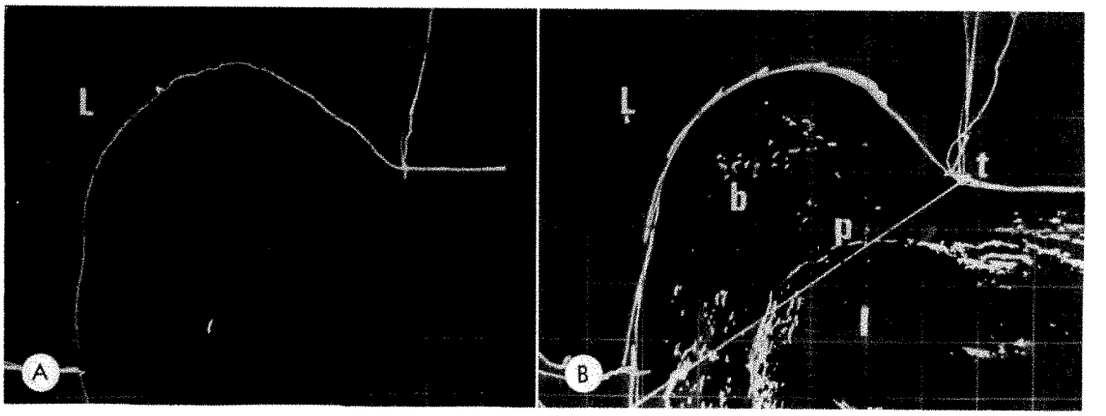


FIG. 3. Case III. *Infiltrating duct type carcinoma of the breast.*

(*A*) Outline of the left breast at the midplane of the treatment field. (*B*) Filled in cross-section of the midplane of the left breast. The treatment beam (t) encompasses the entire breast (b). It skims the pleura (p) with minimal irradiation of the lung (l).

torting the bladder. With the use of the ultrasound scans, anterior and posterior radiation therapy portals were set up (Fig. 1, *A–D*).

The patient died 2 weeks after completion of radiation therapy with pulmonary metastases, local tumor and aspiration pneumonia.

CASE II. E.J., a 26 year old Negro female, was in good health until a nodule was discovered in the right lobe of the thyroid in January 1971. A radioisotope thyroid scan showed a large nonfunctioning nodule in the lower right lobe of the thyroid. In February 1971 she had a right thyroidectomy. The pathologic diagnosis was mixed cell type papillary and follicular carcinoma of the thyroid. Two months later she developed a mass in the left lobe of the thyroid and a palpable lymph node in the right supraclavicular region. Reoperation showed involvement of the left lobe of the thyroid by the tumor and extension into the trachea and strap muscles. A right supraclavicular lymph node also was positive. In view of the extent of involvement, it was elected to treat the patient with radiation therapy.

Ultrasound was used to plan the treatment

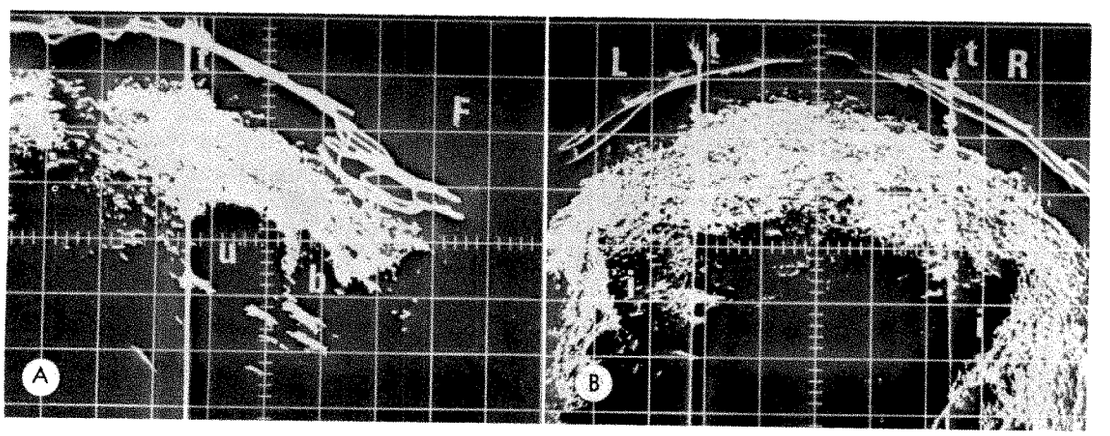


FIG. 4. Case IV. *Adenoacanthoma of the uterus.*

(*A*) Longitudinal cross-section of the midplane of the pelvis. The head of the patient is to the left and the feet to the right of the picture (F). The uterus is at (u) and the urinary bladder at (b). Note that the upper border of the treatment field (t) transects the upper border of the uterus. The upper border was then moved cephalad to encompass the entire uterus. (*B*) Horizontal cross-section through midplane of the treatment field shows that the lateral borders of the treatment field (t) cross the pelvis at the iliac wings (i) encompassing the true pelvis.

fields. Figure 2, *A–D*, shows the ultrasound pictures and resultant computer print out.

Case III. L.B., a 50 year old Negro female, was admitted because of a large, indurated, superficially ulcerated, left breast. One year prior to admission she had a mass in the left breast biopsied with a diagnosis of cystic hyperplasia. The biopsy site failed to heal. At the time of this admission seropurulent and bloody fluid was draining from the breast. Induration extended to the axilla, but no discrete lymph nodes were palpable. The liver was palpable 4 cm. below the right costal margin and had a knobby nontender texture. An isotope liver scan showed multiple defects in uptake. A needle biopsy of the breast proved infiltrating duct type carcinoma of the breast. It was elected to treat the breast with radiation therapy.

Using ultrasound "B" scanning, medial and lateral tangential ports were set up which just

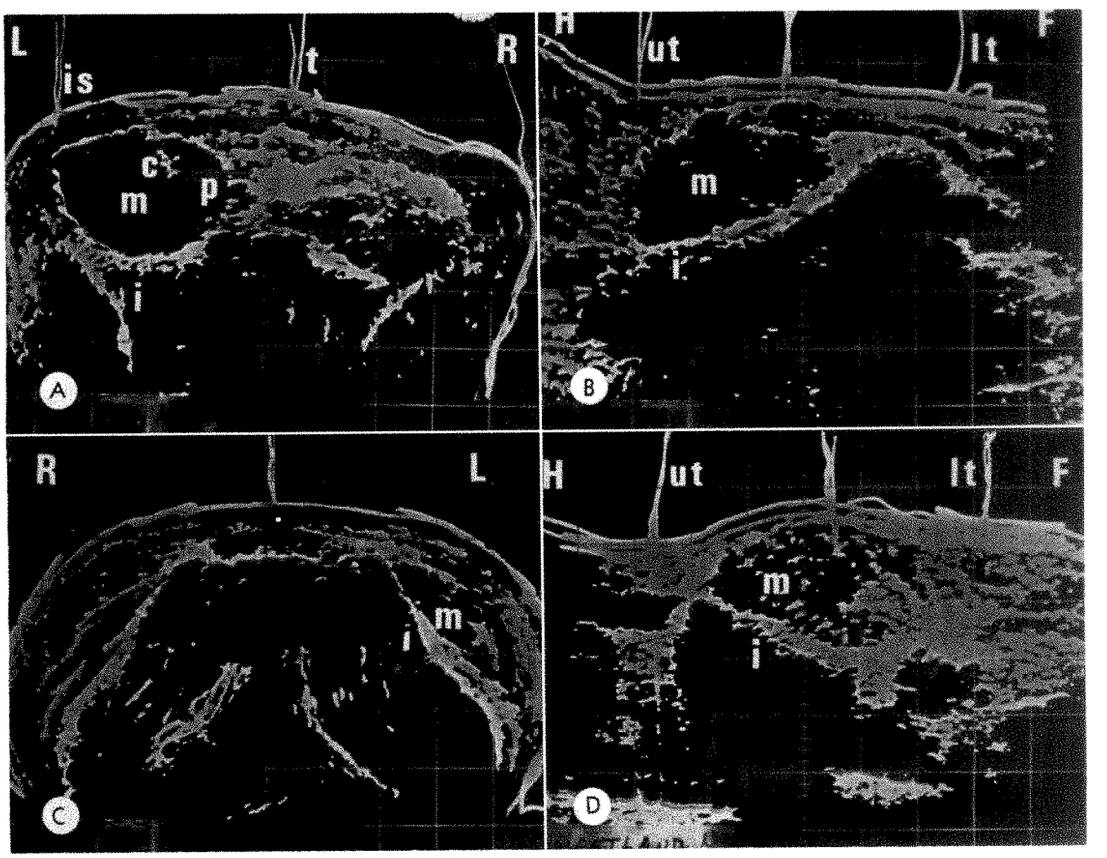


Fig. 5. Case v. *Ewing's sarcoma of the left ilium.*

(*A*) Anterior horizontal cross-section through the midplane of the treatment field to the left pelvis. The tumor (m) is sonolucent but contains a few echoes from an area of calcification (c). The tumor displaces the psoas muscle (p) medially and anteriorly. The anterior iliac spine is marked at (is) and the medial border of the treatment field at (t). The lateral border of the treatment field is the patient's left side. (*B*) Anterior longitudinal cross-section through the vertical midplane of the treatment field. The portion of the tumor (m) located anterior to the ilium (i) is seen to extend slightly cephalad to the upper border of the treatment field (ut). The patient's head is to the left (H). (*C*) Posterior horizontal cross-section at the midplane of the treatment field shows the tumor (m) posterior to the iliac wing (i). The medial border of the treatment field is at (t). The lateral border of the treatment field is the left side of the patient. (*D*) Posterior longitudinal cross-section at the vertical midplane of the treatment field; the patient's head is to the left (H). The upper border of the treatment field (ut) and the lower border of the treatment field (lt) encompass the tumor (m) situated posterior to the iliac wing (i).

skimmed the pleura. The ultrasound is shown in Figure 3, *A* and *B*. In addition, left anterior supra and infraclavicular ports were added.

The patient died suddenly 4 days after therapy was started. An autopsy was not obtained.

CASE IV. K.McQ., a 56 year old white female, presented with a history of irregular vaginal bleeding during the past year. She developed heavy vaginal bleeding 2 days prior to admission. On pelvic examination the cervix was firm with small nodules in the right lateral vaginal fornix. The uterus was enlarged to the size of a 10–14 week pregnancy. The adnexa were normal. Dilatation and curettage, and cone biopsy showed adenoacanthoma of the uterus with invasion of the cervix and vagina.

Initial external radiation therapy was planned to be followed with intracavitary radium therapy. The external anterior and posterior treatment portals were set in the usual manner by palpation and roentgenograms.

These fields were checked with ultrasound "B" scans (Fig. 4, *A* and *B*). They showed that the cephalad border of the treatment fields transected the upper border of the uterus. The treatment fields were then adjusted cephalad to encompass the uterus.

The patient developed lung and liver metastases and died about 2 months after therapy was completed.

CASE V. N.S., a 20 year old white male, noticed increasing swelling and tenderness of the left buttock about 1 year prior to admission. Roentgenograms of the area showed a diffuse sclerosis of the left iliac wing and no definite soft tissue mass. Open biopsy showed a gray non-gritty necrotic tumor involving the gluteal muscles with gross extension into or from the medullary portion of ilium. The pathologic diagnosis was Ewing's sarcoma. There was no evidence of distant spread.

Anterior and posterior radiation therapy portals were set up to encompass the left half of the pelvis and the palpable mass.

These fields were checked with ultrasound "B" scans to determine if the entire soft tissue mass was encompassed (Fig. 5, *A–D*). It was seen that the anterior cephalad portion of the mass was not included in the treatment fields, so the upper border of the field was raised to include all of the mass.

Six weeks after the beginning of therapy the ultrasound scan was repeated showing decrease in the soft tissue mass (Fig. 6).

SUMMARY

Ultrasound scanning can be a valuable aid in radiation treatment planning. It provides an easy and accurate method of obtaining body outlines and cross-sections of the treatment fields. In many cases, ultrasound scanning can delineate the borders of a soft tissue tumor which cannot easily be delineated by other methods. Thus, the changes during and following irradiation therapy can be followed.

Certain limitations in the technique of obtaining cross-sections, that must be pointed out, are the presence of good acoustic interfaces at the tumor margin, the blocking effect of gas filled structures and bone, and the presence of skin incisions. However, in all cases an accurate body outline can be obtained.

It should also be pointed out that pulsed diagnostic ultrasound is painless, innocuous to underlying tissues, and easily applied;

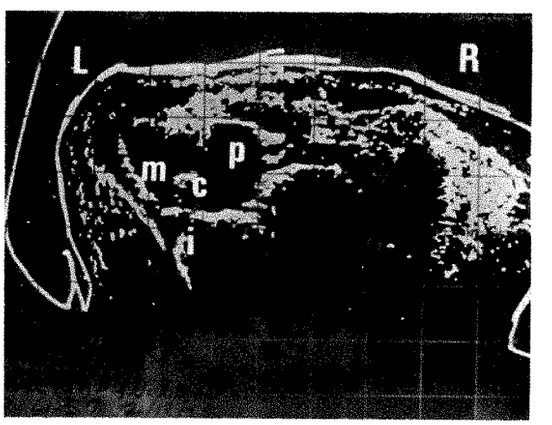


FIG. 6. Case V. *Ewing's sarcoma of the ilium.*
Anterior horizontal cross-section at same level as in Figure 6*A*, done at the end of therapy, shows the decrease in the size of the tumor (m). The calcification (c) has moved closer to the iliac wing (i) and the psoas muscle (p) has returned to near normal position.

thus, ultrasound procedures may be repeated as often as needed.

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AN ELECTROSTATIC PRINTER DISPLAY FOR COMPUTERIZED SCINTISCANS*

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RADIOLOGIC interpretation has conventionally depended upon the inspection of images as recorded on film. The film functions to quantify, store and display the transmission of radiation. Through the introduction of digital computers into nuclear radiology, these 3 elements have been separated, and the computer assigned the responsibility of quantification and storage. Nevertheless, it is still desirable for the radiologist to view scintiscan information in a pictorial form. Until recently, computer produced displays have been laboriously produced and of limited appeal.

With a new development in digital computer peripherals, the electrostatic printer, good pictorial representations can be obtained.

METHOD

Scintiscans were obtained by a Nuclear Chicago Pho/Gamma III scintillation camera and the scintillation data stored in a 64 by 64 matrix format within a Digital Equipment Corporation PDP/12A (8K of core) digital computer. On completion of a scan, the data matrix was transferred to magnetic tape for permanent storage. After unmodified recall or analysis of the matrix, the data were subdivided into equal intervals to match the number of available display shades. Each interval was assigned one shade: 16 shades of gray plus white were used. Patterns of dots, each comprising an area of 8 by 8 fixed size and uniformly spaced dot points, were used to represent shades. The simulation of gray was produced by varying the total dot complement within the prescribed dot point area.

The patterns representing the shades which had been assigned to the data intervals were printed on a Versatec Model 100A electrostatic printer under direct computer control. The location of the overall pattern area was determined by the coordinates of the scan data matrix cell. On some of the displays a grid of the data matrix was simultaneously printed over the data, again under direct computer control.

RESULTS

Electrostatic printer hard copy displays of the Hine Phantom, without and with a superimposed grid, are shown in Figure 1, *A* and *B*, respectively. Each display presents data from a 64 by 64 matrix. Grid spacing of Figure 1*B* is by 2 matrix cells, both horizontally and vertically. A similar display for 2 views of the liver appears in Figure 2. A comparison was made between the scintiphoto and the electrostatic printer display of a liver viewed in the anterior projection with a lead marker placed below the right costal margin (Fig. 2, *A* and *C*) and in the right anterior oblique projection without marker (Fig. 2, *B* and *D*). The patient had an enlarged liver with an irregular distribution of the radionuclide. Both the displays of Figure 1, *A* and *B*, and 2, *A* and *B*, are after the data have been corrected for camera uniformity. A 6 per cent background erase with contrast enhancement was computationally applied before production of the displays of Figure 2, *A* and *B*.

Printing time for any scan without superimposed grid took about 13 seconds. The overlay of the grid marker increased electrostatic printer display time by less than 1 second.

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DISCUSSION

Rectilinear scanners and gamma cameras rely primarily on the exposure-density characteristics of photographic materials to record count density. Film exposed in the proper response range produces an image which accurately quantifies variations in radionuclide distribution and also acts as the display for visual evaluation. Incorrect exposure, however, is a common occurrence and results in incomplete recording and inaccurate quantification. These errors have been eliminated to a large extent by using a computer to relieve film of its function of data quantification.

The computer, when suitably interfaced to an imaging device, can accurately quantify and store data in a count density matrix format. The stored original data can be recalled numerous times for manipulation according to the demands of the clinical decision maker. Computer manipulations can be either corrective or analytic in nature. Important corrective procedures for gamma camera data are adjustments for field non-uniformity,[3] data smoothing of statistical noise and deblurring.[7] Analytical operations involve background or foreground suppression, contrast enhancement, scan subtraction and contour plotting.[4]

Common to all computer manipulations of either unmodified, corrected or selectively analyzed data is that the results are in numerical form. These numbers may be directly printed out for evaluation. The confusion generated by the plethora of information and the unfamiliar form, however, makes it difficult to draw area-related conclusions. Hence, a numerical printout is rarely produced. Instead, some form of pictorial display is constructed based on the relational magnitude of the numbers. This "image" provides a visual means for rapid evaluation of regional quantification.

Basic to popular display techniques is the need to have the imaging mechanism electronically compatible with the computer and to avoid special hardware. One device that satisfies these criteria is the high speed impact line printer. The line

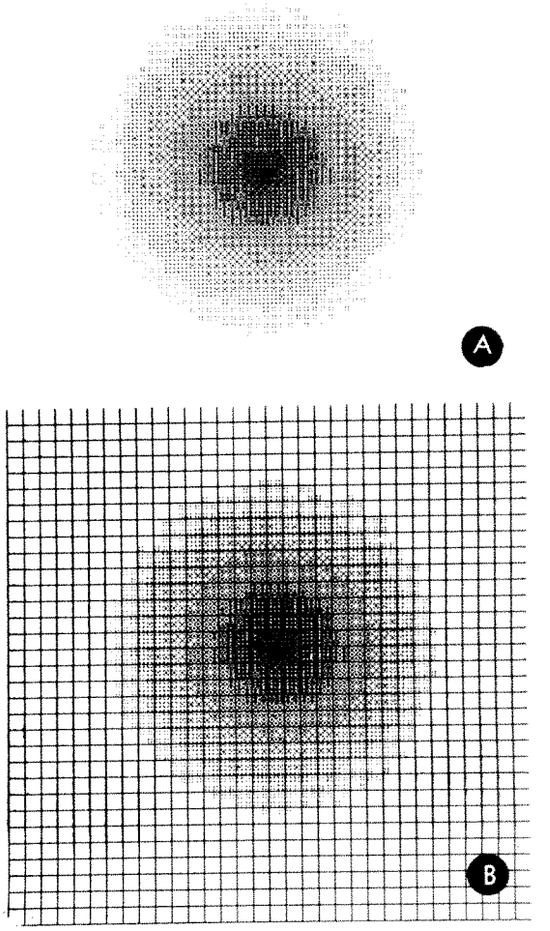


FIG. 1. Electrostatic printer display after uniformity correction of (*A*) the Hine Phantom and (*B*) Hine Phantom with superimposed grid.

width for conventional printers is on the order of 128 to 132 characters. This means that for data matrix widths of 64, 2 characters at most may be used to represent 1 matrix cell. A maximum incremental difference of 1 per cent is numerically provided by 2 characters. Equal magnitude output using the numbers 0 through 9, representing 10 per cent increments, has been tried.[8,12] Because of the large number field still present, however, lines are hand-drawn between each increment to produce a contour-like appearance. The resultant activity map has a geometric form similar to anatomic shape, reduces the complexity of the data map, and makes the net visual ap-

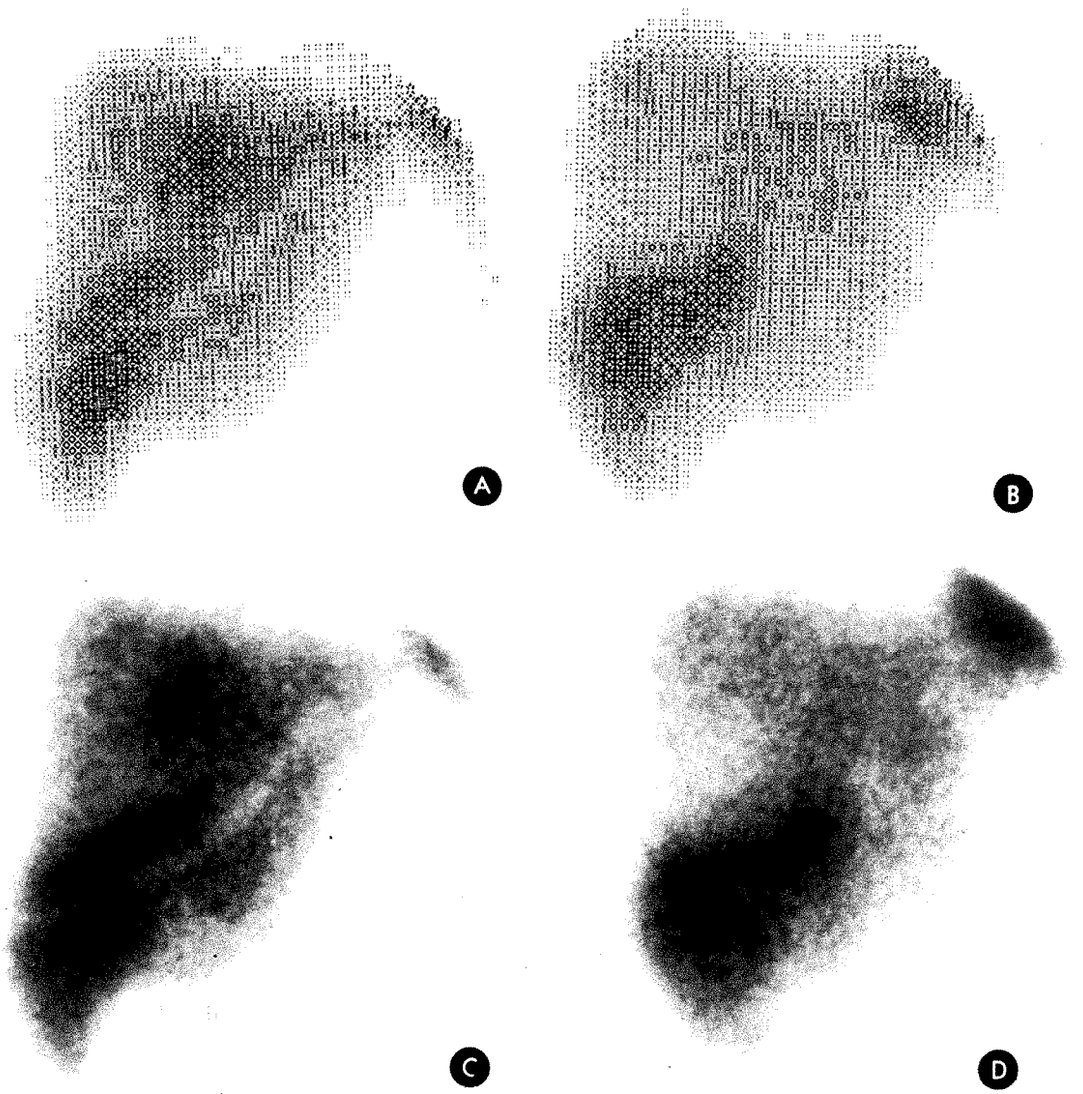


FIG. 2. (*A*) Electrostatic printer display after uniformity correction and 6 per cent background erase with contrast enhancement of anterior view of a liver with a marker wire below the right costal margin. (*B*) Electrostatic printer display after uniformity correction and 6 per cent background erase with contrast enhancement of right anterior oblique view of the same liver without marker. (*C*) Film display of the same anterior view as in *A*. (*D*) Film display of the same right anterior oblique view as in *B*.

pearance easier to interpret. This improvement, however, is at the expense of extra time and effort.

Differing symbols from the line printer character set have also been used, the selection of which is based partly on the apparent visual density of the character. Appropriately dense characters have been used to represent specific data intervals.[10] Because single characters have a limited range of visual densities, repeated ranges simulating graded contours have been produced.[5,8,9] When line printer characters can be overprinted, a more full density range may be produced to eliminate the contour appearance.[3,6,10]

Output time for hard copy of these images is a consideration of importance.

Using a 600 line per minute (lpm) printer, hard copy of a scan can be made in about 10 seconds for equal magnitude or single symbol printout of a 64 by 64 matrix. The printout time for the overprinted displays, while more scan-like in appearance, is anywhere from 2 to 4 times as long, depending upon the number of overprints. Since Polaroid film, the most rapid conventional scan display medium, requires at least 10 seconds for development, line printer wait times for single symbol printouts are not overly long.

One obscure feature of the line printer type of display is the geometric distortion introduced by the unequal character-to-line spacing. Without mechanically altering the printer, there is a 5:6 ratio of horizontal to vertical spacing for a print using 2 characters along its width and a single space between data rows. This often unnoticed difference may be critical when comparing and identifying organ size from the computer printout.

The dominant display mechanism for digital computer scintiscans is the controlled gray image of the monochromatic cathode ray tube (CRT). Three variations of this form of display can be identified. In the first, the coordinates of the matrix element identify a location on the screen. This position is intensified according to the content of that cell and an appropriate gray shading control. This type of display requires 3 low accuracy digital to analog (D/A) converters, 2 at the accuracy of the matrix dimensions to locate the display point and the third at the accuracy of the number of shades to modulate intensity. This form of display is rapidly produced and can, under computer control only, be refreshed often enough, so that the image appears flicker-free with a short persistence phosphor CRT. In the second form of CRT display, the coordinates of the matrix cell again identify a location on the CRT which is, however, repeatedly intensified according to the content of that cell. Only 2 low accuracy D/A converters are required. The excessive computation time for multiple passes over the CRT face dictates the need for a long persistence phosphor or photographic summation. The third type of display requires that the coordinates of the matrix cell locate the corner of an appropriate display area and that a pattern of dots simulating gray shading is displayed within that area. This image form requires 2 high accuracy D/A converters, so that each dot within the display area is discretely controlled. A long persistence phosphor as well as a high resolution CRT is necessary for flicker-free display.

Unlike line printer displays with fixed geometric factors, the CRT display dimensions can be widely varied. True geometric accuracy or purposeful distortion can be readily achieved.

None of the CRT forms provides a direct hard copy. Even though computer stored data can be recalled at any time and although the potential of direct interaction with the display through a light pen or similar device is possible, it is still desirable to have at least one hard copy for inclusion with the patient's record. More important, if subtle manipulative differences are to be compared, evaluation is difficult without side by side displays, either two CRTs or two hard copies.

A permanent record from a CRT display can be made with film. With Polaroid, there is a minimum of a 10 second developing time per film. The development of individual conventional negative films is more time consuming as well as cumbersome. Batch processing of negative film can be done with cine developing equipment, but this delays the objective of having immediate results available after the performance of the scan.

It may be summarized that a display mechanism for computer stored scintiscan data should have the following qualities: (1) the display should be available shortly after obtaining the scan; (2) hard copy of images should readily and quickly be made; (3) the display should have a wide range of gray tonalities; (4) the image should be

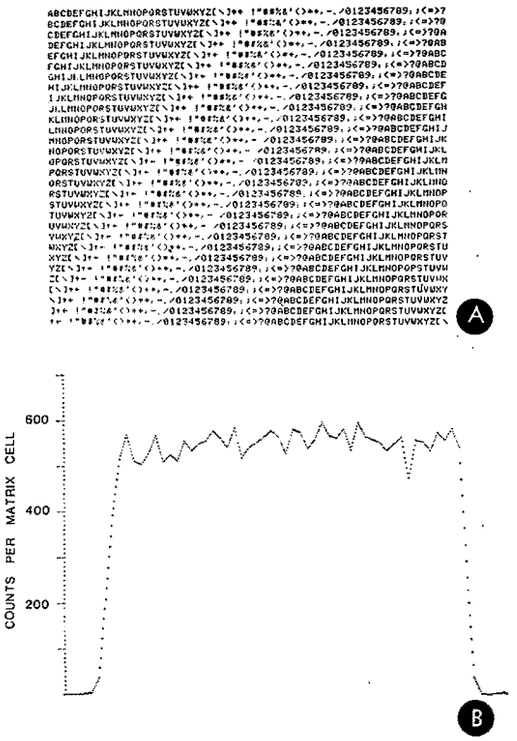


FIG. 3. (*A*) Alphanumeric character set as an example of electrostatic printer dot matrix font. (*B*) Count profile of central row of scintillation camera flood data matrix after uniformity correction as an example of electrostatic printer graphics. Labeling added by hand.

geometrically accurate; and (5) the device should have a standard interface to a digital computer, *i.e.*, computer peripheral. Although unrelated to the quality of the display, but intimately associated with computer operations; (6) the display algorithm should be easy to program; and (7) the peripheral should be inexpensive to purchase and maintain.

These display criteria are generally fulfilled by an electrostatic printer.[2,11] The electrostatic printer (ESP) is a digital computer peripheral that prints alphanumerics in dot matrix form (Fig. 3*A*) and produces low resolution graphics (Fig. 3*B*). The printer is mechanically simple, having only a precision paper drive assembly, but is electronically complex. Since mechanical components are usually the first to break down, the electronic complexity is a satisfactory substitute for mechanical simplicity.

The theory of operation of an electrostatic printer is simple. A drive mechanism moves special paper over a long row of uniformly spaced brushes, or nibs, which may be charged with a high voltage. Paper motion, which is in steps equivalent to the brush spacing, runs perpendicular to the line of brushes. An energized nib charges the paper immediately touching it. At some later stage in the printer processing, the locally charged paper attracts ink particles which flow by in a low concentration suspension. Uncharged paper does not attract ink and so remains white.

With only one row of nibs, intricate timing is required for decoding alphanumeric data into letters which cover multiple rows. This complexity, however, can be handled by digital circuitry and is a built-in feature of the printer. No further demands on the program or programmer are required other than to supply alphanumeric code in the normal manner at a high rate of speed. Slower electrostatic printers output alphanumerics at rates of approximately 300 lines per minute, while faster devices print as high as 4,800 lpm, a rate of output well beyond the capabilities of most mechanical line printers.

The electrostatic printer may be used in place of a digital pen recorder for graphics. Curves, however, must be drawn as scan rasters from either a large storage buffer or by a sophisticated program. With either method of ESP raster generation, plotting time can be made to approach paper drive time, so that the most complex contour plot, isometric projection or graph can be drawn in the time used to advance the paper past the row of charged nibs, or about 15 seconds for an 11 inch page on the slowest model. Although the plotting time for a pen type plotter is much longer, control is easier. Pen type plotters also have better resolution. ESP drawings with dot

resolution of 70 to 100 dots per inch, depending on the model, can be compared to graphics of pen plotters having 200 increments to the inch.

The shade of gray display program developed for the electrostatic printer is a variation of the plotter operation. The number of shades, pattern size, dot count and location of the dots within each pattern is the prerogative of the program designer. Since data must be scaled to match a selection of gray shades and since dividing by 16 is computationally convenient on a mini-computer without a hardware divide, only 16 shades plus white were used; and, since the computer output is by 8 bit bytes per output command, 8 by 8 dot matrix patterns were most convenient. The increment of dots from one shade to the next is 4. The linear increase in dot count per pattern is arbitrary and could be made logarithmic to simulate the exposure-density characteristics of film. The location of each dot within the pattern area is also arbitrary, but a smoother appearance of the over-all image is obtained when the dots are uniformly spread. While the total number of dots representing one shade is fixed, the pattern is not. Fixed patterns can sometimes be visually disturbing in that a large area of the same pattern can produce striping (shades 3 and 9 in Fig. 4*A*). As has been suggested for a CRT display,[1] random placement of dots within the matrix at display time would avoid this striated appearance. Striping, however, only becomes apparent over large contiguous areas of the same gray shade and is not the usual case with scintiscan data. A simulated step-wedge of the selected patterns appears in Figure 4*A* with the exact dot locations appearing in the enlarged version of Figure 4*B*.

The 8 by 8 dot patterns are coarse but so, in general, are the data. With a 70 dot per inch electrostatic printer, a 64 by 64 matrix of numbers will cover a 7.1 by 7.1 inch area with 0.114 inch squares for each matrix cell. For proper visual impact, the image should be either minified or viewed from a distance beyond which individual dots and patterns are not discernible. The reproductions of Figures 1, 2, and 4 are minified slightly by the publication.

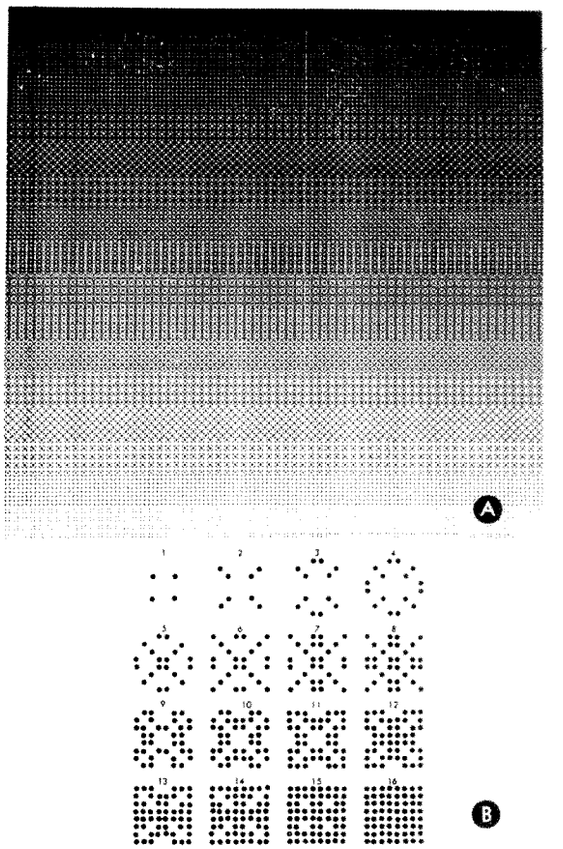


FIG. 4. (*A*) Simulation of photographic step wedge using dot patterns. (*B*) Enlargement of dot patterns.

SUMMARY

An electrostatic printer is a digital computer output device that combines the capabilities of rapid alphanumeric printing and, using suitable software, full plotter-like graphics.

It can also be used to produce good simulated shades of gray for the display of scintiscan data.

That these three forms of hard copy output can be made by a single peripheral makes an electrostatic printer a desirable

piece of equipment in a nuclear medicine and computer complex.

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VOL. 117, NO. 1

Co^{60} SIMULATOR

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STRIPPED to essentials the specification for a simulator is that it shall be an x-ray machine specifically designed to produce visible records portraying the path which proposed beams of therapeutic radiation will take relative to a patient's tumor and neighboring anatomic structures. To accomplish this the diagnostic instrument must be able to match mechanically the various movements of radiation source relative to patient in a particular therapy unit or by making adjustments to match such movements in several different units. A popular concept is that simulators must "duplicate the geometry" of the therapy units with which they are teamed. We shall see presently that this ideal is impossible of accomplishment in the case of Co^{60} units and that certain ill-advised attempts in that direction are impractical.

In the matter of "visible records" the question arises as to whether they should be films alone or films plus fluoroscopy by means of image intensifier tubes with television viewing. For almost all the work simulators are called on to do, films alone suffice. It is argued that T.V. fluoroscopy is an important time saver, but the provision of a small film processor adjacent to the simulator speeds up filming and costs far less than T.V. fluoroscopy.*

PENUMBRA

Because the radiation emitted by Co^{60} units and the x-ray tubes of simulators arises in multiple points rather than a single point, the beams from both are bordered by partially illuminated fringes known as penumbra.† The width of penumbra (Pn) depends on the diameter of the source (S), the distance of the source from the final collimator (D) and the distance from the final collimator to the surface on which the beam impinges (d), the relationship being expressed in the equation $Pn=(S\times d)/D$. In our equipment $S=0.2$ cm. for the x-ray tube and $S=2.0$ cm. for the Co^{60} unit. D is fixed at 65 cm. and d is variable from 15 cm. for the upper surface of a patient's body located at the rotational axis to 35 cm. for the exit surface of such a patient having a body thickness of 20 cm. to as much as 40 cm. for x-ray film in a tunnel beneath the therapy table. Our penumbra widths range, therefore, from 0.46 mm. to 1.07 mm. to 1.23 mm. for the x-ray beam and from 4.6 mm. to 10.7 mm. and 12.3 mm. for the Co^{60} beam.

The earliest simulators were used with linear accelerators having radiation sources approximately identical with those of the x-ray tubes in the simulators. Today most simulators are used with Co^{60} units and the relatively broad penumbra widths inherent in the latter make it impossible to accomplish the "duplication of geometry" which had come to be looked on as an essential feature during the work with linear accelerators.

SUGGESTED COMPENSATION FOR DISPARITY IN SOURCE DIAMETER

Some writers have suggested that by juggling the distance between source and "port" (final collimator), the disparity between penumbra widths of the 2 beams might be made to interfere less with accomplishing "identical geometry." Figure 1, however, shows that 2 such suggestions fail to accomplish the intended purpose, and instead introduce errors of their own.

The only acceptable arrangement is to mount both sources with identical distances from source to "port" (D) (Fig. 1, Case 1). In this situation the x-ray beam includes part, but not all the penumbra of

*Our instrument was constructed in the Bio-Electronics shop of the University of Florida, most of the mechanical and electrical work be ing done by Charles Rabbit and Fletcher Stephens.

†We consider "penumbra" a sound term in this connection despite contrary arguments of some pedants.

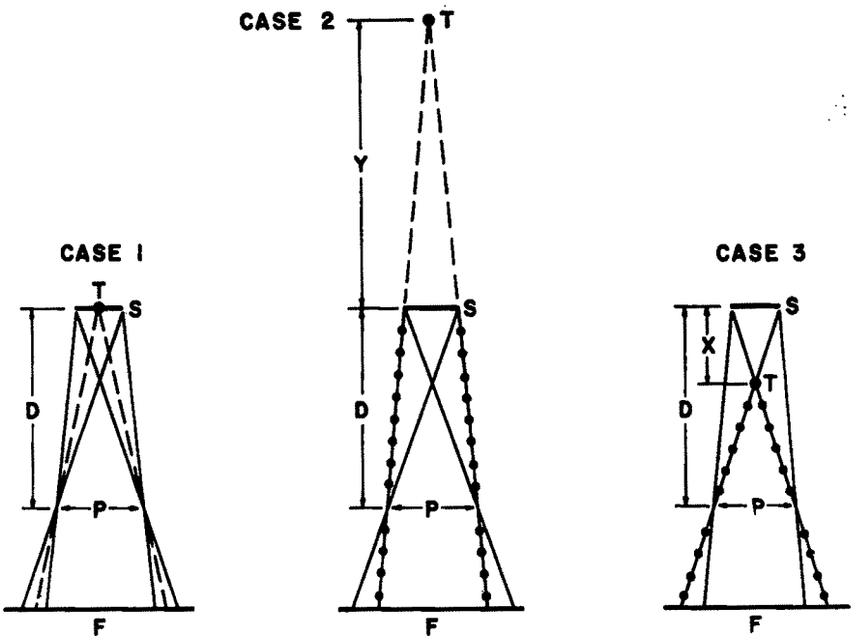


FIG. 1. *Geometry of Image Production by Co^{60} and X-ray Beams (arbitrary scale).*

When the opening or port (P) in a lead block is placed on the blocking tray of a Co^{60} applicator and a simulated port of the same dimensions is placed on the tray of a matched simulator, the resulting film images (F) will have obvious penumbra in the case of the Co^{60} beam with its 2 cm. source (S) and negligible penumbra in the case of the x-ray beam with its 0.2 mm. source (T).

When the 2 sources are equidistant from the blocking tray (Case 1), the x-ray beam includes part, but not all the penumbra of the Co^{60} beam. It is generally agreed that this is the most satisfactory arrangement.

Raising T above S by the amount Y (Case 2) makes for inconvenience and increased expensiveness of equipment, and the exclusion of all penumbra it accomplishes has no therapeutic advantage.*

Dropping T below S by the amount X (Case 3) includes all penumbra, but this, too, is without therapeutic advantage.*

When dimensions S, D and P are known, X and Y can be computed from appropriate equations, both values being independent of the distance of the radiation source from the film or of the blocking tray from the film:

$$Y = \frac{SD}{P - S}; \quad X = \frac{SD}{P + X}.$$

* For additional practical disadvantages of Case 2 and Case 3, see Figure 2.

the Co^{60} beam, regardless of the diameter of the "port" (P).

For any particular value of P there is a distance (Y) above the Co^{60} source which when occupied by the target of the x-ray tube will assure that the x-ray beam just fails to include any of the Co^{60} penumbra (Fig. 1, Case 2). Such an arrangement has actually been suggested, even though it necessitates constructing a pit or a bridge. Aside from construction cost and operating inconvenience, the arrangement is unsound, first because there is no merit in excluding all Co^{60} penumbra and second because Y would have to be adjusted for varying values of P (Fig. 2). For a P larger than the one for which Y was calculated, the x-ray beam would fall short of the inner edge of the Co^{60} penumbra and for a smaller P, include some of that penumbra.

Another suggestion is that the x-ray target be lowered by the amount (X) be-

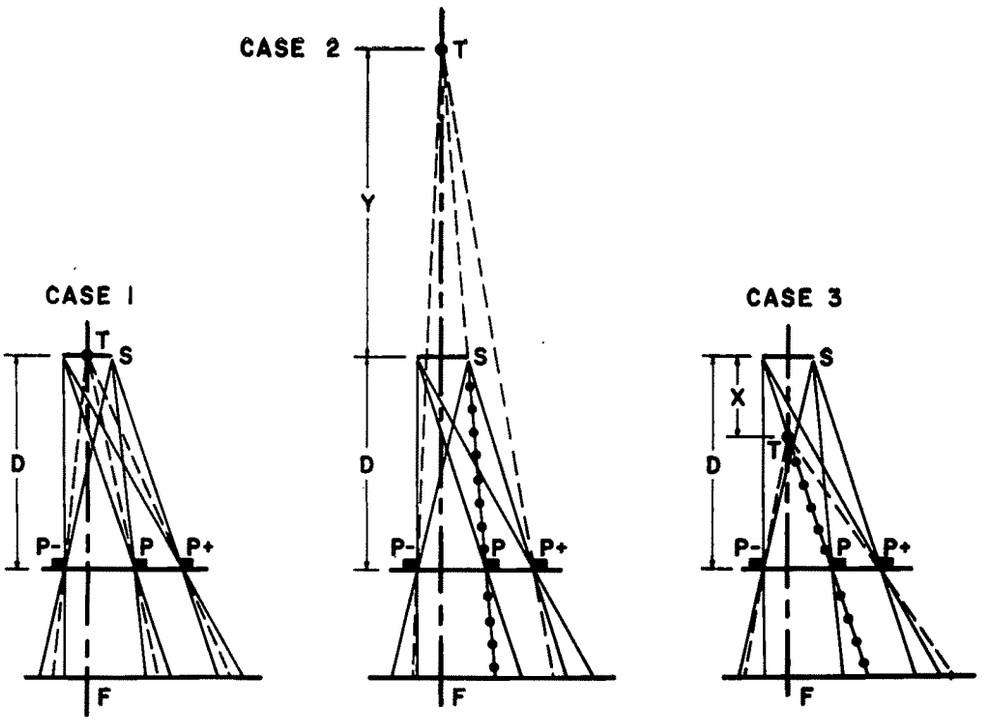


FIG. 2. *Dependence of Beam Geometry on Port Size* (arbitrary scale). ——= Co^{60} beam; – – – –= X-ray beam; –·–·–·–·–·–= both beams.

Technical Note. To right of center (P) designates right-hand edge of port from which X and Y were calculated, and (P+) the right-hand edge of a larger port. To the left of center (P−) designates the left-hand edge of a smaller port.

Case 1. When S and T are equidistant from the port, the x-ray beam includes half the Co^{60} penumbra, regardless of port size.

Case 2. When S remains at distance D, but T is raised to D+Y, the outer edge of the x-ray beam coincides with the inner edge of the Co^{60} penumbra only for port size (P). For (P+) it excludes not only penumbra, but part of the penumbra-free beam as well. For (P−) the reverse occurs, and the x-ray beam includes part of the Co^{60} penumbra.

Case 3. When T is dropped below S to the point D–X, the outer edge of the x-ray beam coincides with the outer edge of the Co^{60} penumbra only for port size (P). For (P+) it extends beyond the outer edge of the Co^{60} penumbra and for (P−) includes only part of that penumbra.

low the level of the Co^{60} source (Fig. 1, Case 3). This would assure that for a particular P and a particular X, the x-ray beam would include all the Co^{60} penumbra. This would have no clinical advantage, would make operation difficult, and unless X were modified for changes of the P, the employment of a larger P would cause the x-ray beam to extend beyond the outer border of the Co^{60} penumbra, while a smaller P would cause it to include only part of that penumbra (Fig. 2).

EQUIPMENT AND ACCESSORIES

These are illustrated in Figures 3 through 6 and described in the accompanying legends.

ALIGNMENT OF PARTS

While one must be philosophical about the impossibility of compensating for disparity between the diameters of the sources of the 2 beams, complacency as to optical matters that are within one's control

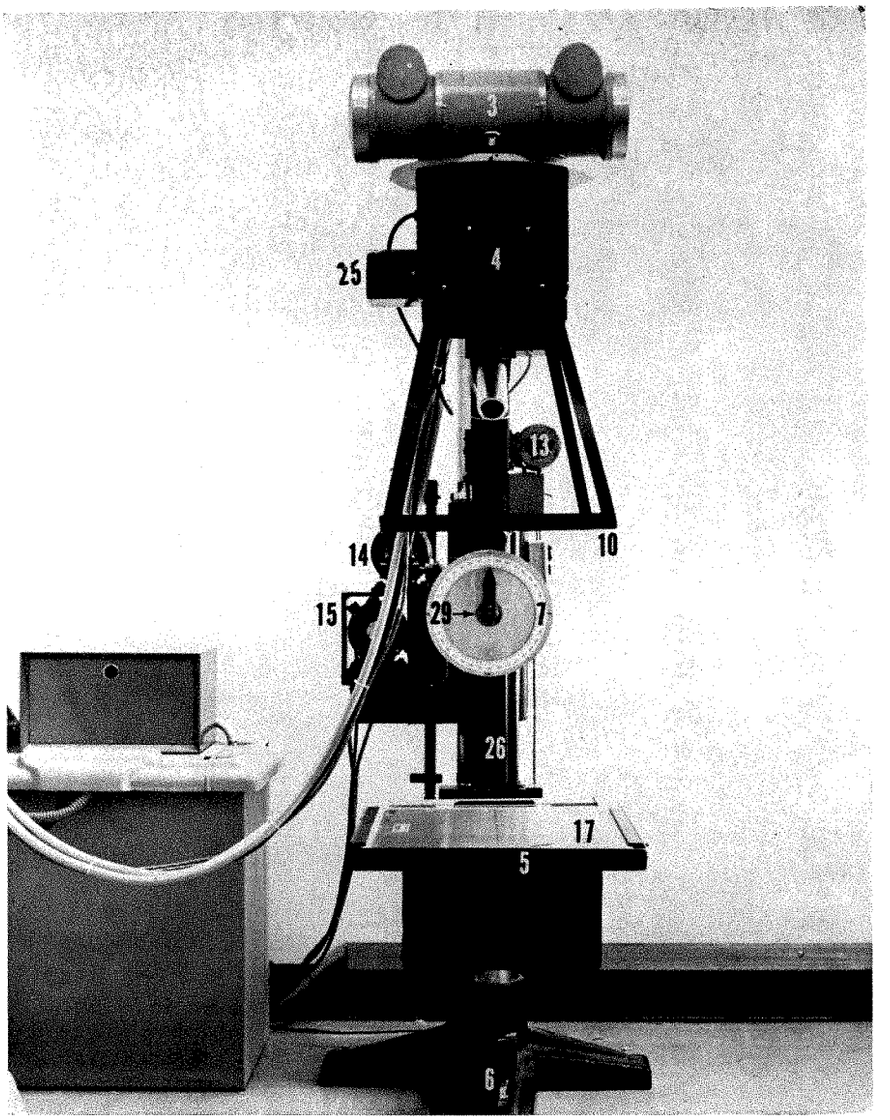


FIG. 3. *General View of Simulator with Arm at "O" Degree.* Target of x-ray tube (3) lies 5.2 cm. above surface of radiation port. Collimator (4) attaches to tube by means of turn-table. Housing for light localizer (25) limits rotation of turn-table to 45 degrees in one direction, but allows 90 degree rotation in the other. In this view the turn-table is at "0" degree. A motor driving a worm which threads through a nut anchored to the bed raises the bed or lowers it, target-film distance being indicated by a scale (26). Angular position of the arm is indicated by protractor (7) and a fixed pointer attached to an axle, the center of which (29) is the axis of the system. The tube arm together with the numerous parts attached to it is raised and lowered by motor (14) and rotated by motor (15). A 6 inch diameter mast passes through the casting which carries axle, arm, etc., and is set in a cast iron base (6) bolted to the floor.

The blocking tray (10) is easily attached to or detached from the collimator. Target-axis distance is 80.7 cm. and target-tray distance 65.4 cm.*

* For our particular Co^{60} unit, the nominal values are given as 80 cm. and 65 cm., but because actual measurements show them to be slightly greater, we have used the latter values for the simulator.

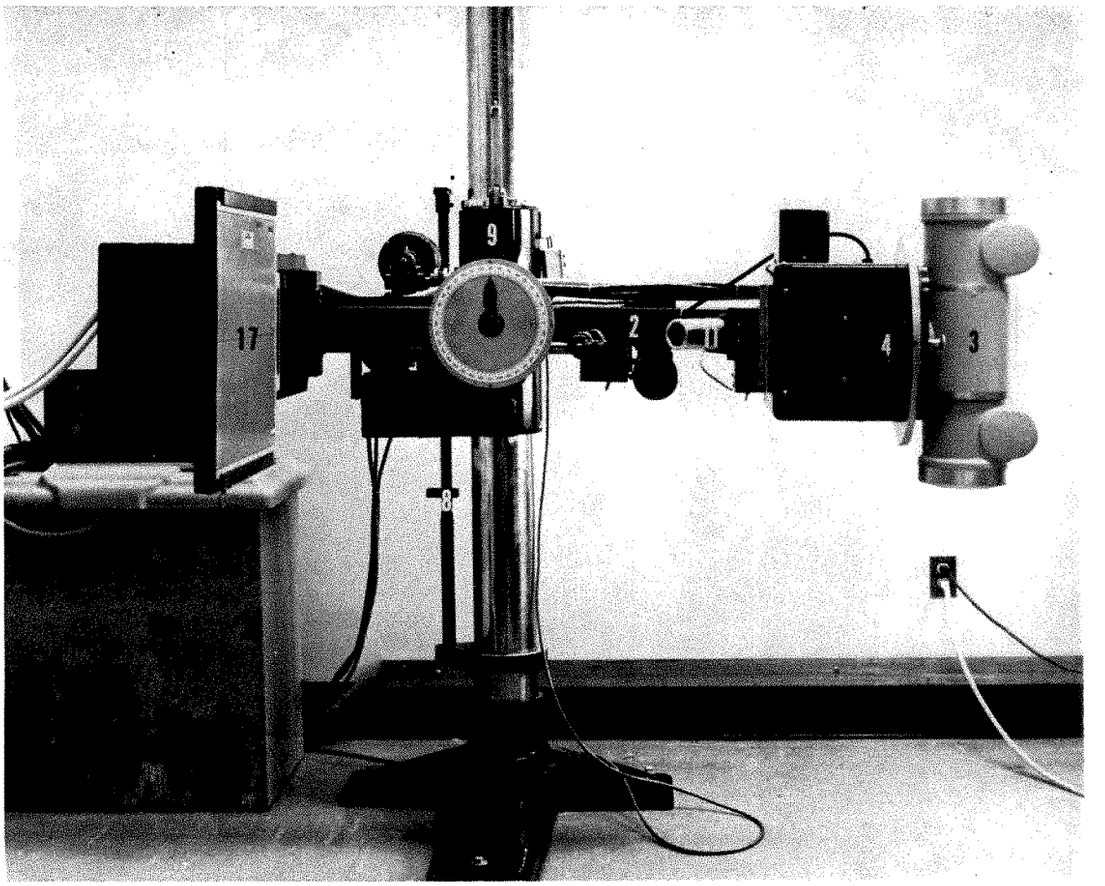


FIG. 4. *Simulator in Position for Cross-Table Film.*

A massive cast housing (9), riding on a 6 inch diameter mast, carries the axle, tube arm (2) and the many parts attached to the arm. A worm (8) attached to the mast by means of a bracket, passes through a captive nut driven by the elevating motor, and because the assembly is counterweighted a small motor suffices for this work. The x-ray tube (3) is bolted to a steel plate secured to the tube arm, and the collimator (4) attaches to the other side of that plate by means of a turn-table. A Picker light scale indicates target-skin distance, that value being read at the point where the image of the scale intersects the image of the transverse axis of the light localizer.

In this illustration the collimator stands at "0" on its rotational scale, but for certain procedures it may be rotated 45 degrees or more from "0". The grid (17) forms the front of the grid-tunnel assembly into which films are inserted. Adapters in film trays assure that, regardless of film size, film centers will coincide with the intersection of long and short axes of the tunnel.

cannot be tolerated. Merely to assure that dimensions and movements of the simulator match exactly those of the therapy apparatus is not enough. The center of the film tunnel must be brought exactly to the foot point of the axis of the x-ray beam, the x-ray shutters similarly aligned and finally the light beam localizer adjusted, under optical control, until the illuminated rectangle cast by the shutters coincides exactly with the fluorescent rectangle presently cast by x rays on a fluoroscopic screen. Failure to do this may introduce errors in clinical application greater than those inherent in disparity in the diameters of the two sources. Shutters and

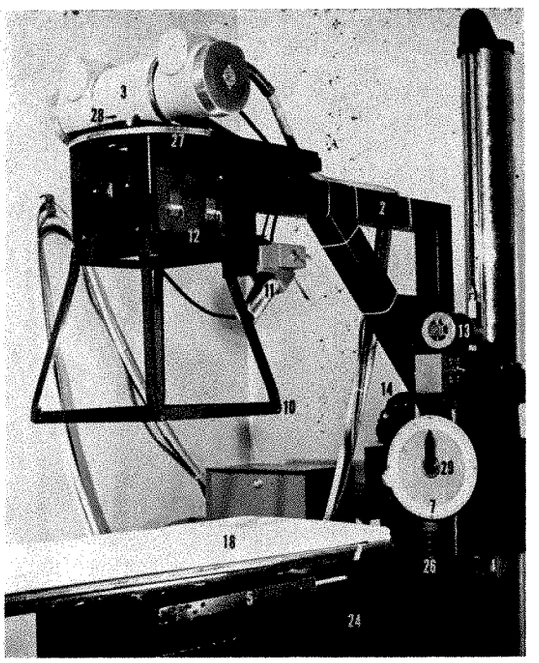


FIG. 5. An x-ray tube (3) is bolted to tube arm (2) with its focal spot 80.7 cm. distant from the axis, which is at the center of the axle (29). The bed (24) which carries the grid-tunnel assembly (5) can be elevated or lowered relative to the axis by means of a motor (13), and its position in space is indicated by the scale (26) calibrated in target-film distance. This latter distance does not enter into the matching of simulator and Co^{60} settings, but, of course, must be known in calculating exposure time for filming.

The tube arm, together with the several parts attached to it, can be raised or lowered by means of a motor (14), and another motor, which does not show in this view, rotates the arm, the degree of rotation being indicated on a protractor (7).

The collimator (4) containing shutters which define x-ray and light-localizing beams is attached to the plate carrying the x-ray tube by means of a turn-table. A lock (28) holds rotation of the collimator in the "0" position, but for special situations it can be rotated, the amount of rotation being indicated on a scale (27). The shutters are operated by knurled wheels (12).

Attachable or detachable from the bottom of the collimator is a blocking tray of clear plastic, (10), the upper surface of which lies 65.4 cm. below the target. A Picker light scale (11) is calibrated to read target-skin distance in centimeters.

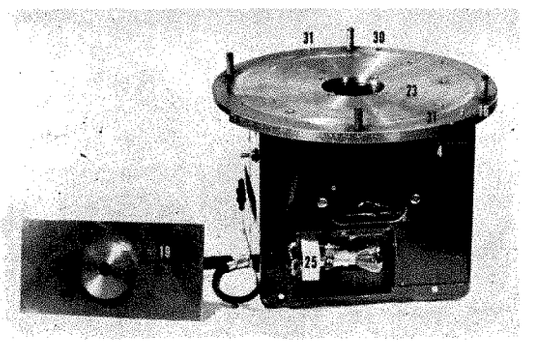


FIG. 6. *Details of Collimator and Beam Indicator.*

The collimator (4) is attached to the inner brass disk of the turn-table (23), which is carried by an outer steel ring (16). The effective target of the x-ray tube lies 5.2 cm. perpendicularly above the center of the lower surface of the radiation port in the housing. We have attached the tube housing to a steel plate (shown elsewhere) with the center of its port precisely aligned with the center of an opening through that plate and carefully aligned with the center of the entrance port of the collimator.

The turn-table and attached collimator are fastened to the steel plate (20; Fig. 7) by 4 steel studs (30) passing through oversized holes, and when the centers of tube-port opening in steel plate and opening in brass disk have been brought into good mechanical alignment, nuts are tightened on the studs and 2 small dowels (31) are installed to assure precise alignment whenever it becomes necessary to remove and replace the collimator.

The lamp of the light localizer has been mounted on a nylon block (25) provided with a drive screw. In this view, covers have been removed from windows in the sides of the collimator through which one reaches to adjust cables which drive the shutters during the final stages of alignment, presently to be described.

The beam indicator (19) is a $12\frac{1}{2}$ inch length of $\frac{1}{2}$ inch O.D. aluminum tubing pressed into a hole through an aluminum disk $\frac{3}{8}$ inch thick and $2\frac{1}{2}$ inches in diameter. The tube is precisely perpendicular to the surface of the disk. Screwed to the disk is a piece of aluminum sheet, the thickness and diameters of which are not critical. The use of the beam indicator is explained in Figure 7.

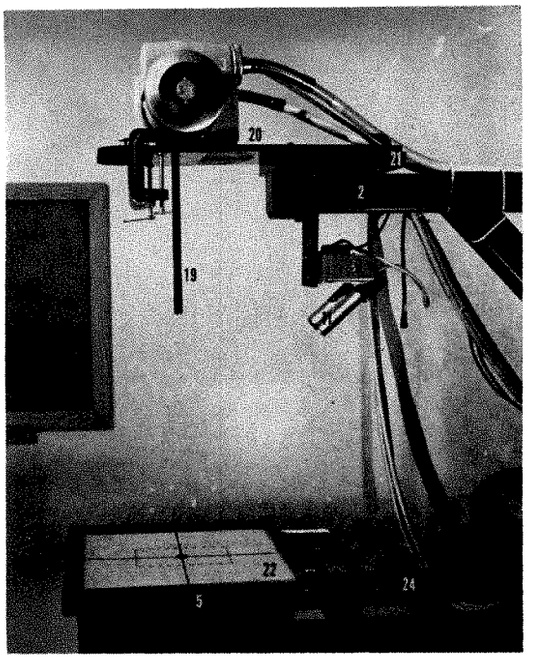


Fig. 7. *First Stage of Alignment.*

The collimator has been replaced by the beam indicator (19) inserted into circular opening in steel plate and secured with "C" clamps. The grid-tunnel (5) lies on the bed (24), but has not yet been screwed to it. A fluoroscopic screen has been taped to the grid and covered with clear sheet plastic (22) on which have been drawn in solid lines the long and short axes of the film tunnel. By means of cellophane tape, a metal washer has been attached to the intersection of the 2 axes. (The rectangle drawn in broken lines, although shown here, actually is not drawn until later in the process of alignment; see Fig. 8.)

To facilitate precise trimming of target-axis distance, the aluminum spacer (21) is employed. Resting on the arm (2) and supporting the plate (20) this spacer can be made thicker to increase or thinner to decrease target-axis distance. The light scale (11) is calibrated to read in target-skin distance.

With ambient light level low and the operator's eyes dark-accommodated, fluoroscopy is begun, employing low kv. and ma. A pencil-like beam of x rays passing down the bore of the beam indicator (19) produces a small spot of fluorescence approximately the size of the washer. When spot and washer are brought into coincidence, the center of the x-ray film will lie directly beneath the x-ray source. Such coincidence is accomplished by shifting the grid-tunnel on the bed and, if necessary, rotating it until its long axis is parallel with the long axis of the bed. When alignment has been attained, the film tunnel is first clamped and then screwed to the bed.

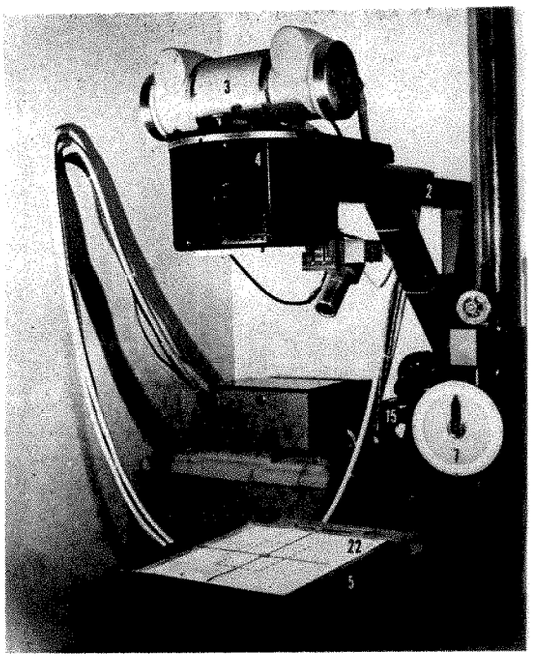


Fig. 8. *Second Stage of Alignment.*

The beam indicator has been replaced by the collimator (4) and fluoroscopy is resumed, the shutters being almost completely closed so that only a small central beam of radiation escapes. If this beam does not exactly coincide with the metal washer, one reaches through ports in the sides of the collimator, adjusting shutter cables until coincidence is attained.

Rectangular lead markers (not shown here) are placed on the plastic-covered screen and the shutters opened to obtain a fluorescent rectangle of some stipulated dimensions. Under fluoroscopic control the markers are moved into position to define the margins of the fluorescent rectangle, and with x-ray "off" and lights "on" the boundaries indicated by the markers are inked in with broken lines.

It remains only to assure that the visible light rectangle from the light localizer does in fact define the area presently to be subjected to x ray. If on testing the visible light rectangle is displaced transversely relative to the broken lines defining the fluorescent rectangle, one introduces a screwdriver through a hole in the collimator housing and turns a screw which tilts the mirror, thus shifting the location of the light rectangle. If the latter is displaced longitudinally, one uses a screwdriver to turn the screw which shifts the localizer lamp longitudinally (see Fig. 6, 25).

light-beam localizers designed for conventional diagnostic x-ray equipment do not lend themselves to precise alignment unless

they have been modified with that work in mind. The means of accomplishing alignment are described in the legends of Figures 7 and 8.

SUMMARY

The specification for a simulator is that it shall be an x-ray machine specifically designed to produce visible records portraying the path which proposed beams of therapeutic radiation will take relative to a patient's tumor and neighboring anatomic structures.

A popular concept is that simulators must "duplicate the geometry" of the therapy units with which they are teamed. This is impossible of accomplishment in the case of Co^{60} teletherapy units.

The authors describe in detail a Co^{60} simulator, designed in the experimental shop, which is simple, inexpensive and advantageous to use.

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NEW METHODS TO FACILITATE RADIOTHERAPY PLANNING AND TREATMENT, INCLUDING A METHOD FOR FAST PRODUCTION OF SOLID LEAD BLOCKS WITH DIVERGING WALLS FOR COBALT 60 BEAM*

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OVER the past several years we have been trying to meet the challenges in radiotherapy planning and treatment by improving available methods and materials. We have had some success, which is reported below. We hope that those therapy centers which have similar problems may find some of our innovations useful.

I. FAST PRODUCTION OF INDIVIDUALIZED SOLID LEAD SHIELDING BLOCKS SHAPED TO MATCH THE DIVERGENCE OF THE SUPERVOLTAGE THERAPY BEAM

Since the acceptance of extended field therapy for Hodgkin's disease to achieve higher cure rates, the divergence of the therapy beam has brought with it the problem of adequate shielding for normal tissues. The handling of thick lead is very difficult. In attempts to cut out shaped blocks from a lead slab, the softness and low melting temperature of the lead makes the saw blade stick.[4] Other methods have, therefore, been developed in which lead shot mixed with liquid plastic material is poured into individually formed molds.[3,8,11,18]

The sides of these molds are usually straight.[2,4,7,9,18] The making of plastic molds where the side walls follow the diverging therapy beam is more difficult[1,3] and may require the purchase of special apparatus.* All these procedures are more time-consuming than desirable.

In most radiotherapy centers, the divergence of the beam is usually ignored, and the lead shields are made thinner, *e.g.*, 5 cm. for cobalt 60, which minimizes the effect of the geometric penumbra.[12] Such shields, however, transmit more radiation (4.8 per cent) than does 7 cm. thick lead (1.4 per cent). This extra radiation to the normal tissues, however small, with today's widespread concern over radiation exposure, is not quite acceptable to many. The straight side walls of the thicker blocks, however, allow transmission through their upper edges, while the corresponding lung areas remain deceivingly camouflaged by the portal light shadow.[10]

In cooperation with the Phelan Manufacturing Company,† an attempt was made to find ways to rapidly produce compact lead shields with sufficient thickness (*e.g.*, 7 cm. for cobalt 60), but with walls which conform to the diverging beam precisely according to their location in the portal. This goal was finally reached when we found a lead-bismuth alloy (3 per cent Bi), the one used in the printing industry, to be most suitable for cutting. This alloy is poured into a slab of any desired thickness (*e.g.*, 7 cm.), which can be cut efficiently and with a band-saw having a 6 teeth per inch blade with angle adjustment. This allows the cutting blade to follow the prescribed "tailor-made blueprint." The latter

* "Therashield," Modern Electronic Diagnostics Corp., Libertyville, Ill.

† Phelan Manufacturing Company, Minneapolis, Minnesota.

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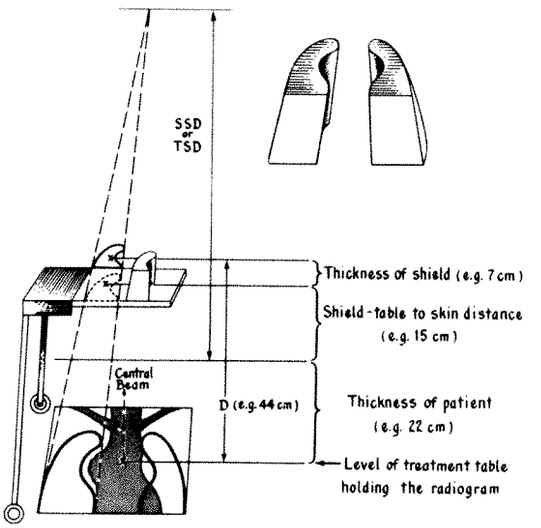


FIG. 1. A method of drawing "blueprints" for shaped compact lead shielding blocks with walls that follow the diverging supervoltage beam (see the text).

can easily be transmitted to the workshop via telephone.

The method is as follows:

1. A radiograph of the patient (*e.g.*, chest) is taken with the treatment equipment (cobalt 60) at the desired source skin distance (SSD) or target skin distance (TSD). The point of central beam is marked on the patient's skin by a thick lead shot.

2. On this radiograph, using a red crayon, the desired contour of the shield is now drawn, outlining the lungs to be shielded, *e.g.*, around a protruding mediastinal mass.

3. This radiograph is placed on the treatment table at a distance determined by: SSD plus the diameter of the patient (*e.g.*, 100 cm.+22 cm.=122 cm.). The central beam is aligned with the marker shadow on the radiograph (Fig. 1).

4. While viewing the radiograph through the plastic shield-table ("shadow tray"), one draws with crayon on the plastic surface the contour of the desired lead block by following the crayon-contour on the radiograph.

5. The shield-table is now lowered by the desired shield thickness, (*e.g.*, 7 cm.). A second contour using a dotted line is drawn on top of the previous drawing by again following the visible radiographic contour.

6. This double contour is now copied onto a transparent paper and the thickness of the shield recorded.

7. The distances between selected reference points on the top and bottom contours are measured (a, b, c, etc., Fig. 2) and are easily utilized to determine the saw-blade angle, as shown in Figure 3.

8. From these data, the shields can now be rapidly cut. The top contour is transfered to the lead slab, having the same thickness used in the "blueprints." The reference points with their corresponding degrees of slope are also marked on this contour. Two persons do the cutting. One changes the angle of the band-saw continuously by following the marked degrees at the reference points, while the other holds and moves the lead slab (Fig. 4).

In lung shields, sometimes the same anterior pair of shields can be used for the posterior portals when reversing the right and left shield. In cases of asymmetry, a different pair of shields for the posterior portal must be made (Fig. 5). In time, one

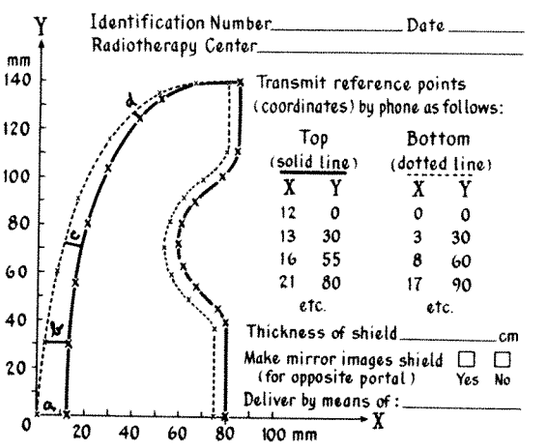


FIG. 2. The "blueprints" ready for telephone transmission using the XY coordinate system. The reference point differences (a, b, c, etc.) in widths between the top and bottom contours allow the determination of the saw-blade angle as shown in Figure 3.

will have a collection of various shields, and there will be less need for additional orders. The shaped shields also can be cut vertically into interchangeable segments which allow more economical use of the shields on hand. The small content of bismuth in the lead does not change the transmission by any practically measurable degree.

As the author is a radiotherapy consultant for a distant community radiotherapy center (Dakota Midland Hospital in Aberdeen, South Dakota) he has put the above method into practical use by ordering such shaped shields by telephone. An ordinary coordinate system is utilized (Fig. 2). The key XY coordinates are given separately for the top and the bottom. The transmission takes only minimal time. At the receiver end, the coordinates are redrawn on a graph paper and any error in transmission of the figures will show up immediately as an unlikely distortion of the contour. An immediate inquiry corrects this error. If more sophisticated visual telecommunication systems are not available, the above method provides a satisfactory replacement.

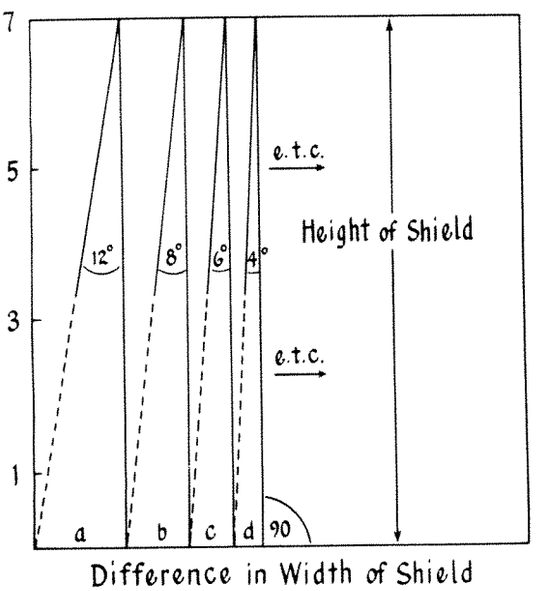


Fig. 3. By using the difference in width (a, b, c, etc.) between the reference points of the bottom and top contours of the shield in Figure 2, the saw-blade angle is easily found (12°, 8°, 6° etc.) by simple geometry as shown above.

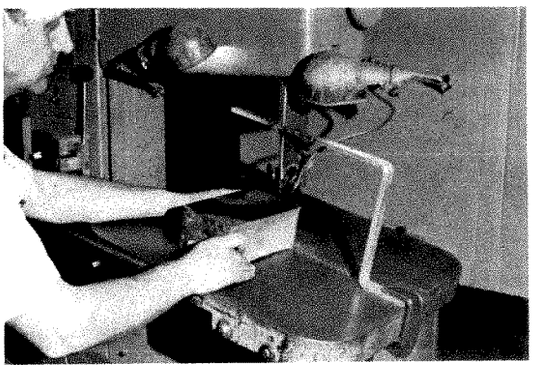


Fig. 4. The top contour of Figure 2 has been transferred to the previously poured slab of lead. The reference points (a, b, c, etc.) are marked on this pattern with their corresponding blade angle (from Fig. 3). One person moves and guides the lead slab, while the other (not seen in this picture) is constantly changing the band-table by using a long handle to cause the blade to follow the pattern in its designated changing tilt.

II. A Technique of "Combined Portal Filming"

Due to the Compton effect, the bone structures are not sufficiently seen on supervoltage radiographs, and barium and iodine type contrast media are rendered useless.[5,13,17] This becomes especially evident when used in below-diaphragmatic wide field portals for the treatment of lymphomas. The image of the lymphographically opacified lymph nodes is lost when using the supervoltage beam, which may lead to inadequate radiation coverage of the lymph nodes. The estimated portals often do not include those lymph nodes which are asymmetrically located or lie outside their usual location; on the other hand, normal structures may be irradiated unnecessarily.[6] The same supervoltage "burn-out" effect is present in organs opacified by barium, *e.g.*, the esophagus. However, the now universally used double exposure technique with lead screened cassettes[13,14] is very satisfactory in the head and neck region, and in the mediastinal area the supervoltage beam has

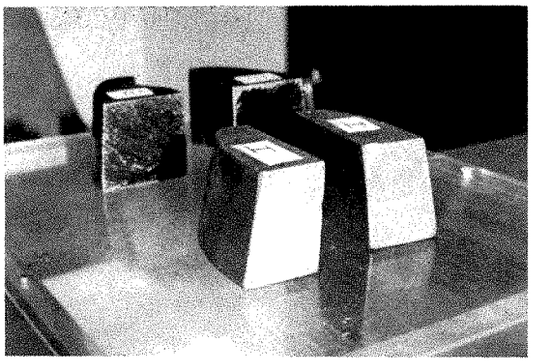


FIG. 5. A selection of compact, 7 cm. high lead blocks with divergent walls for lung shielding. They can be produced rapidly in "tailor-made" fashion. When sliced vertically, they may often be used in combination for different patients or melted and re-utilized.

provided even certain advantages due to its penetrating power.[15–17]

In order to overcome the first mentioned handicaps and because our radiotherapy department has not yet obtained a therapy simulator, a simple effective "combined filming" technique was developed. This also may serve as a double check for the simulator set-up under actual treatment conditions as needed.

The method is simple:

A roentgenographic exposure covering a larger area than the treatment portal is made with portable roentgen-ray equipment, or with the accessory roentgen-ray tube mounted on the rotatory cobalt 60 unit. This exposure is made at the same distance as the planned SSD. A second double exposure is made in the treatment position, using the supervoltage beam which, however, has to be attenuated by a lead shield. Either a grid or non-grid cassette is used, depending on how fine detail is desired. We now mainly use a flexible, thin roentgen-ray holder (GAF Anscoflex Exposure Holder*) which can be easily slipped under the patient or taped alongside his body. Industrial type films are not used; we replaced them with regular medium speed roentgenographic films. Lead screens were not found necessary, nor did they seem to add to the excellent results obtained when using high speed intensifying fluorescent screens (Radelin TF 2†) alone.

The first roentgen-ray exposure is made, using the regular roentgenographic technique with appropriate factors adjusted to the SSD. The supervoltage exposure is made in the treatment position through an attenuating lead shield placed below the collimator. The thickness of the lead varies from 0.5 to 2 cm., depending on the output of the cobalt 60 or supervoltage roentgen-ray unit. The needed exposure at chosen SSD after attenuation is about 0.3–0.5 r. The variation in thickness of the patient does not appear to affect the image quality significantly. The basic image is produced by the first background roentgenographic technique, while the supervoltage beam simply shows the exact portal coverage (Fig. 6; and 7).

III. A QUICK WAY TO MAKE PATTERNS OF IRREGULAR SUPERFICIAL TREATMENT FIELDS FOR LEAD SHEET CUT-OUTS

1. A contour is drawn with a felt-tipped black pencil around the skin lesion, marking the desired treatment field.

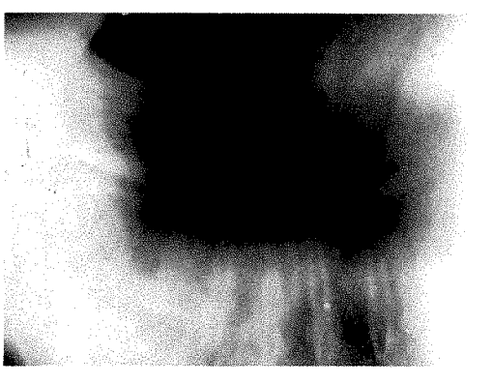


FIG. 6. Barium filled esophagus with cobalt 60 portal mapped for rotational therapy. The technique of "combined portal filming" described in the text allows evaluation of not only the dark supervoltage portal, but also the bone structures needed for orientation. Barium or iodine opacified organs are not "burned out" by the supervoltage beam.

* GAF Corporation, New York, New York.

† Radelin Division, United States Radium Corporation, Morristown, New Jersey.

2. A transparent tape, such as Scotch Magic Transparent Tape #810* is pressed over this contour and the adhering print carried over to the lead sheet, where it remains clearly visible for cutting (Fig. 8, *A* and *B*). In case of a larger lesion, the tapes can be arranged side by side to provide a larger surface. We have found this method especially useful when the skin surface and the contour both are irregular, such as encountered with canthal and nasal epitheliomata.

IV. A NEW MOLDABLE BOLUS MATERIAL

Another challenge for the radiotherapist has been the need for an easily moldable water-density material which follows the contours of any irregular body surface but remains solid at body temperature.



Fig. 7. The value of the "combined portal filming" technique is clearly evident in this patient with Hodgkin's disease. This technique reveals that only borderline coverage of the right lateral retrocrural lymph node is present, resulting in inadequate radiation therapy. The loin shields were swung out on both sides to correct the inadequacy. With such precise portal mapping, more bone marrow can be saved from needless irradiation. (Courtesy of Dr. H. J. R. MacDonough, Dakota Midland Hospital, Aberdeen, South Dakota.)



Fig. 8. (*A* and *B*) An ink marked contour of an irregular superficial therapy portal over an uneven body surface can easily be transferred onto the lead shield for a cut-out.

We have experimented with wax-like materials composed of acetylated monoglycerides and have finally decided on a mixture which fulfills the above criteria. Two commercially available products are used. They are: (1) Myvacet, Type 5-07,† an hydrogenated cottonseed oil with about one-half acetylation of the hydroxyl groups —three parts; (2) Myvacet, Type 700,† an hydrogenated lard with about $\frac{2}{3}$ of the hydroxyl groups acetylated—one part. This mixture has the desirable density of 1.02 g./cm.^{3}.

Besides being useful in orthovoltage therapy, 5–6 mm. thick sheets can be made by pouring this melted mixture into a teflon or silicone treated pan. Suitable pieces can then be cut from the slab and molded over

* Minnesota Mining & Manufacturing Co., St. Paul, Minnesota.

† DPI Division, Eastman Chemical Products, Inc. Minneapolis, Minnesota.



FIG. 9. A certain mixture of acetylated monoglycerides provides an easily moldable water-density bolus material for use in radiotherapy. It is useful with ortho- as well as supervoltage beams. This illustration demonstrates a mold made from a 6 mm. thick slab shaped to fit the chin. Such thickness is useful in cobalt 60 teletherapy to bring maximum electron build-up to the skin surface in those cases where the deep-lying malignancy has reached the integumentum.

the treatable area (Fig. 9) when using the cobalt 60 beam; this is very useful when one wants to bring maximum electronic build-up to the skin level, as when treating deep tumors which have reached the skin surface. We have found it useful to wrap the mold in an ultra thin plastic sheet before each treatment to protect it against soilage. Such materials, sold for household use, serve this purpose well.

Most radiotherapists have to encounter one problem or another brought about by their particular equipment or its physical setup, or by other specific needs. It is hoped that the above methods and materials may benefit those faced with problems such as we have had in the past.

SUMMARY

The author describes: (1) a rapid method to produce solid lead shielding blocks with divergent walls to follow the supervoltage beam, which can be ordered from the workshop by a telephonic "blueprint" code; (2) a technique of supervoltage "combined portal filming" to avoid "burn-out" effect of the barium or iodine opacified organs; (3) a quick way to make patterns for irregular lead cut-outs in superficial therapy; and (4) a new moldable tissue density bolus material.

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EFFECT OF SHADOW TRAYS ON SURFACE DOSE AND BUILD-UP FOR MEGAVOLTAGE RADIATION*

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BESIDES higher depth dose, the main advantage that megavoltage radiation has over orthovoltage radiation in the treatment of deep-seated tumors is the skin-sparing effect. This is due to the finite distance required for electronic build-up in the tissue. Theoretically, the dose at the skin surface should be negligible, but this is never achieved because the x-ray or gamma-ray beam always contains electrons scattered from the collimator of the teletherapy unit and from the air above the patient. The skin therefore does receive some finite dose, although usually too small to cause any harsh reactions. The depth of the maximum dose depends of course on the energy of the radiation, and for 6 MV. x rays, which will be the main thrust used in this paper, the depth is usually taken to be 1.5 cm.

This skin-sparing effect of megavoltage radiation is, however, lost to some extent when a plastic tray for supporting beam-shaping blocks is attached to the source head. The plastic is a copious source of secondary electrons generated by the primary radiation, and these electrons, travelling in the forward direction, increase the dose to the patient undergoing treatment. The depth of penetration of these electrons cannot exceed the depth at maximum electronic build-up, and thus an increase in dose occurs in the superficial tissue supposedly benefiting from megavoltage radiation. A number of studies have been carried out on various aspects of this so-called electron contamination[1,3,6] and this paper reports our findings chiefly for 6 MV. x rays from a Varian Associates Clinac-6.

EXPERIMENT

Figure 1 represents schematically our experimental set-up. A stack of 1 inch thick lucite blocks was placed under the collimator of the teletherapy unit. Additional thin sheets of lucite, of thicknesses $\frac{1}{32}$ inch and more, were placed upon this stack for measuring build-up. The surface was always adjusted to be 100 cm. from the source.

The shadow tray was of lucite $\frac{5}{8}$ inch (1.5 cm.) thick. It was held rigidly in place by means of aluminum brackets attached to the collimating head, so that its lower surface was always 29 cm. from the surface of the phantom. It was inconvenient to place the shadow tray any farther away from a patient if all treatments were to be carried out at source skin distance (SSD) of 100 cm. The thickness was such that it very likely absorbed all electrons scattered off the collimator.

For some of our measurements we used an electron filter consisting of a sheet of lead $\frac{1}{32}$ inch thick, which we taped immediately under the shadow tray when necessary.

For dosimetry we used TLD-100 lithium fluoride powder, whose linearity and consistency had already been checked. This powder was placed on small strips of thin tracing paper (0.05 mm. thick) in uniform layers 0.2 mm. thick. These strips were either laid out flat on the surface of the phantom, or folded over once and placed under 1 of the thin lucite sheets in the path of the central axis of the beam. Only 1 strip was irradiated at a time. The read-outs were plotted against depth in lucite and a

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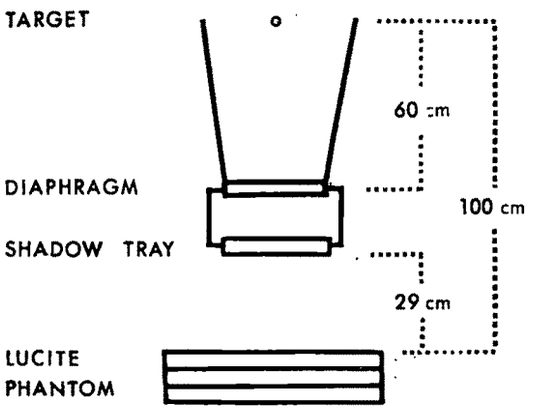


Fig. 1. Experimental arrangement for measuring build-up for 6 MV. x rays.

smooth curve was drawn. From this curve the maximum dose was determined and was used for calculating percentage depth doses.

6 MV. X RAYS

Measurements were made: (a) without the lucite shadow tray; (b) with the tray; and (c) with the tray and the lead filter, in each case for field sizes from 5×5 to 25×25 cm. Also, for a fixed field size, we investigated the effect of varying the thickness of the lucite in the x-ray beam, and the results from different kinds of shadow trays.

Some of the results are shown in Figures 2, 3 and 4. These indicate how increasing the field also increases the dose both at the surface and over the first few millimeters. The reason is, of course, increased electron scattering from the diaphragm, air and the phantom itself. The same reason also explains the apparent shift of the depth of peak dose to shallower levels for larger fields. For the 5×5 cm. field this depth is 15 mm., while for the 25×25 cm. field it is 10 mm.

The build-up curve for a small field (Fig. 2) implies that the true depth of maximum dose for the uncontaminated x rays occurs at about 14 mm., and that, therefore, all percentage depth doses should be calculated with respect to this point, even for

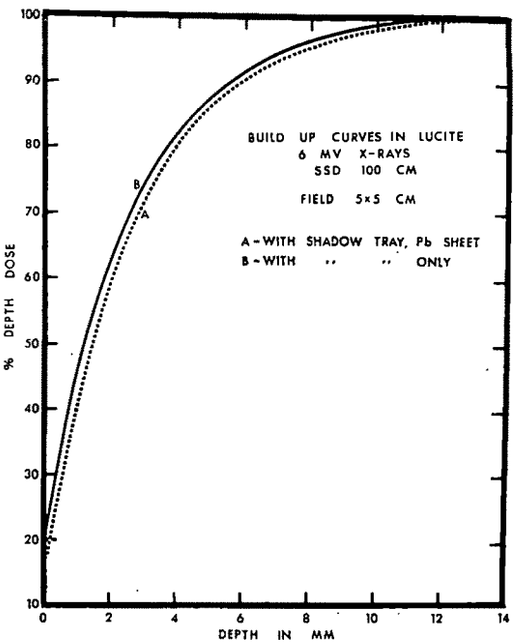


Fig. 2. Build-up curves showing effect of lead sheet in filtering out electrons in the x-ray beam.

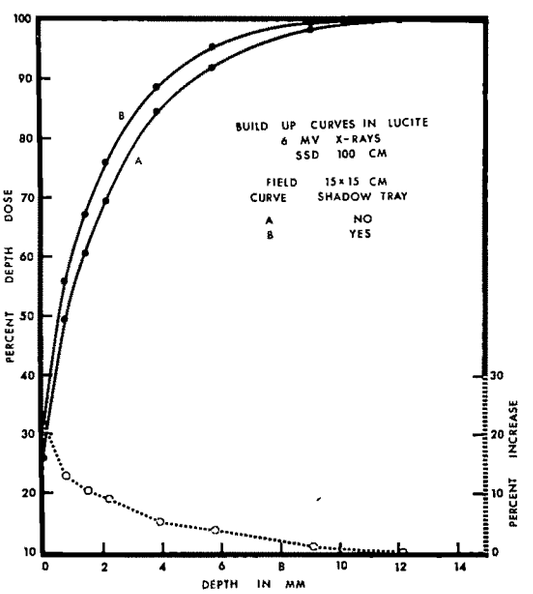


Fig. 3. Build-up curves showing the increase in dose due to electron contamination from the lucite shadow tray. The dotted curve represents per cent increase in local dose, and is to be referred to the dotted scale on the right.

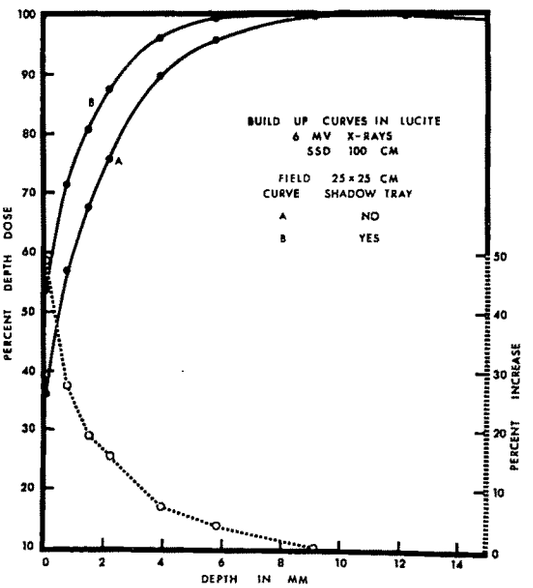


FIG. 4. Build-up curves showing the increase in dose due to electron contamination from the lucite shadow tray. The dotted curve represents per cent increase in local dose, and is to be referred to the dotted scale on the right.

large field sizes. Since contaminating electrons are unlikely to travel this far, such a depth dose will give a true measure of the effect of contamination, especially when comparing the doses with and without the shadow tray, and at different field sizes. However, we have determined that for large fields the dose varies so slowly in the range of 10–15 mm., that we can take the 100 per cent point at whatever depth the maximum dose occurs, with negligible error.

Figure 2 shows the effect of electron contamination in a small field. Both the curves A and B were measured with the shadow tray in place, but for A the lead filter was included. The filter obviously has an effect. Over the first 4 mm. there is a drop in percentage depth dose of about 4 per cent. In the case of the open beam, that is without any shadow tray or lead filter, the curve lies between A and B, but so close to B that it has been omitted for the sake of clarity. From this we conclude that: (a) the collimator generates some contaminating electrons; and (b) the shadow tray, when in place, absorbs these electrons, but gives rise to about the same number in the exit beam. This is not the case for larger fields, as shown in Figures 3 and 4. In both figures, curve A refers to the open beam, where the only electron contamination is from the diaphragm and the intervening air, while curve B, with the shadow tray in place, excludes the diaphragm electrons but includes contamination from the tray and the air. There is a definite increase in superficial doses. For the 15×15 cm. field, the surface dose increases from 26 to 32 per cent of the maximum dose, and for the 25×25 cm. field the increase is from 37 to 53 per cent, which is a 48 per cent increase in local dose. While fields as large as the latter are usually used in conjunction with lead shielding blocks which reduce the effective area of irradiation, nevertheless these figures are indicative of the maximum effects produced.

The build-up curves pertaining to the lead filter have not been shown in Figures 3 and 4. In Figure 3 such a curve would have been just under A, indicating that the lead efficiently stops the electrons from the shadow tray and can even lead to superficial dose levels better than those from the open beam. In Figure 4, the curve would have almost coincided with A, meaning that enough electrons are being scattered

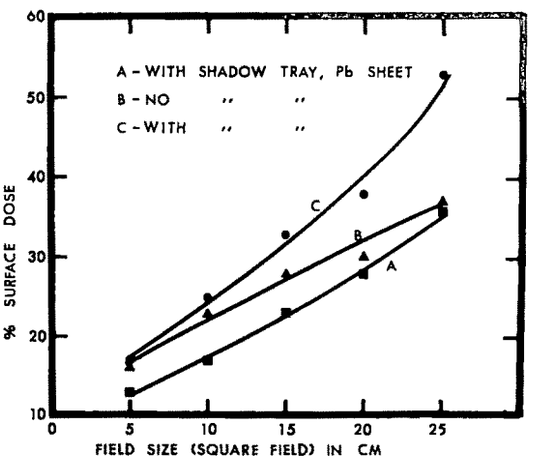


FIG. 5. Percentage surface doses for 6 MV. x rays in lucite phantom, source skin distance (SSD) 100 cm.

off the lead itself to match those off the collimator in the open beam. Of course, the bulk of electron contamination for large fields probably comes directly from the overlying air.

Figure 5 shows at a glance the variation of surface dose alone with field size, especially the large increase produced by the shadow tray at larger field sizes. Also seen is the effectiveness of the lead sheet in reducing the surface dose.

Frequently, patients are treated using the isocentric technique where the tumor is 100 cm. from the x-ray source. The skin of the patient is even closer to the source, perhaps as little as 85 cm. away from it. The shadow tray, if in place, is then only 14 cm. from the patient, so that the electron contamination from it would be expected to produce a larger dose in the skin. This was confirmed in a set of measurements that we made with a masonite phantom, where only the percentage surface dose was measured for 2 SSDs. The results are shown in Figure 6.

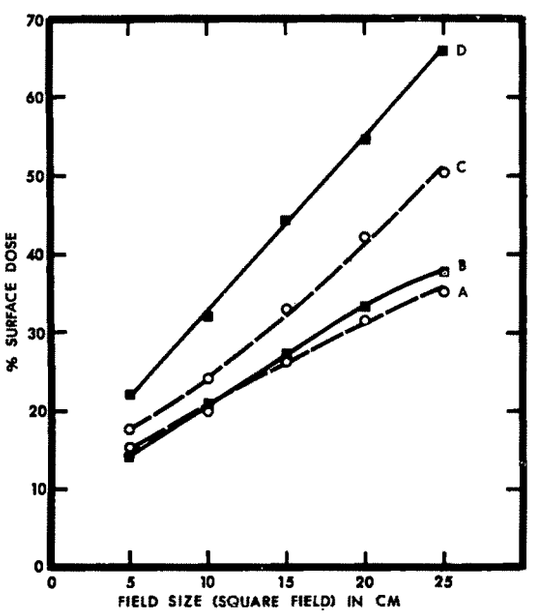


Fig. 6. Percentage surface doses for 6 MV. x rays in masonite phantom. A-SSD 100 cm., and B-85 cm., without shadow tray. C-SSD 100 cm., and D-SSD 85 cm., with lucite shadow tray.

We then tried to determine what effect the thickness of the plastic shadow tray had on the amount of electron contamination. For this, the field size was fixed at 25×25 cm., and varying thicknesses of lucite were placed at a height of 29 cm. above the phantom. For each thickness the percentage surface dose in the phantom was measured. The results are displayed in Figure 7, and they show that an approximately $\frac{1}{4}$ inch thick sheet of lucite at 29 cm. height is sufficient to produce the maximum electron contamination. This is the least thickness necessary to support the lead blocks. Greater thicknesses serve only to strengthen the shadow tray, while attenuating the x rays to some extent.

Finally, a set of measurements was carried out to determine how different kinds of shadow trays affected the surface dose. Figure 8 shows the results. As mentioned earlier, the largest reduction in surface dose occurs if a lead sheet is attached under the shadow tray, when the depth dose curve almost coincides with A. If no such electron filter is used, then the best shadow tray is one that offers the least obstruction to the x-ray beam, and in our case consists of a wire mesh made from nylon wire 0.055 inch thick in a $\frac{1}{2}$ inch mesh. This was only 18 cm. above the phantom when measurements were made, but the increase in surface dose is found to be quite small when compared with that due to the solid lucite tray. This fact has been noted by others.[4] Build-up curves were also measured with lead blocks arranged in a typical treatment pattern on both the lucite and the wire mesh shadow trays, and a similar decrease in superficial doses was noted with the latter tray.

2 MV. X RAYS AND COBALT 60 GAMMA RAYS

A complete set of measurements were also carried out on a 2 MV. Van de Graaff unit (made by High Voltage Engineering Corp.), where for an SSD of 100 cm. the distance from the lucite shadow tray to the phantom was 42 cm. Because of this great distance, the electron contamination and consequently the increase in superficial dose

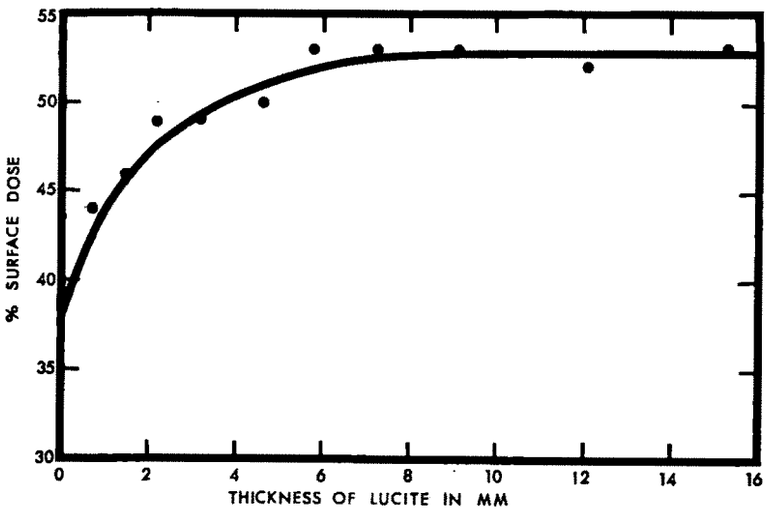


FIG. 7. Variation of percentage surface dose in lucite phantom with thickness of lucite interposed in 6 MV. x-ray beam.

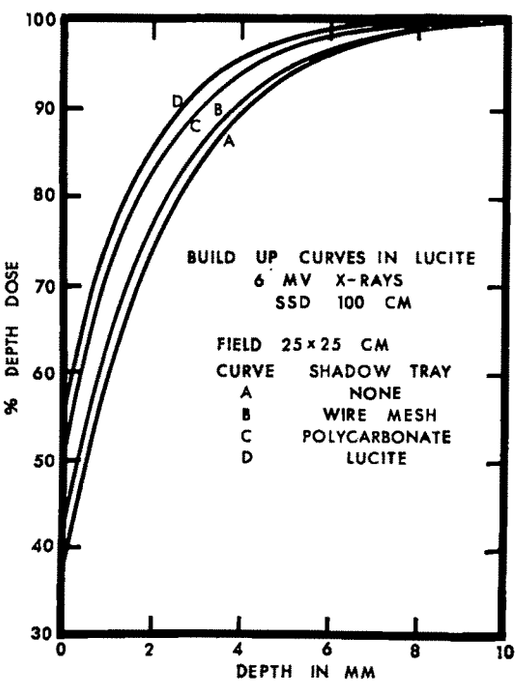


FIG. 8. Build-up curves for 6 MV. x rays for different shadow trays. A-none. B-nylon wire mesh, 18 cm. from phantom. C-polycarbonate, 3/16 inch thick, 29 cm. from phantom. D-lucite, 29 cm. from phantom.

were very small even at the large fields. However, the numerical values of percentage surface dose were comparable to those from the 6 MV. unit with its lucite shadow tray in place. For example, for a 25×25 cm. field these values were 58 per cent and 53 per cent for the 2 MV. and the 6 MV. units, respectively (Fig. 9), while for smaller fields the figures were farther apart but still comparable. Thus the shadow tray reduced the skin-sparing properties of the 6 MV. x rays almost to those of the 2 MV. beam.

For purposes of comparison, build-up curves were also measured on an AECL Theratron 80, cobalt 60 unit. For an SSD of 80 cm., the diaphragm was only 15 cm. and the plastic shadow tray only 11 cm. from the phantom. Both are less than the generally recommended distance of 20 cm., so that high electron contamination was expected, and found. One set of data is shown in Figure 10 to illustrate the seldom discussed peaking effect in the shape of a build-up curve when large contamination is present.[2,5]

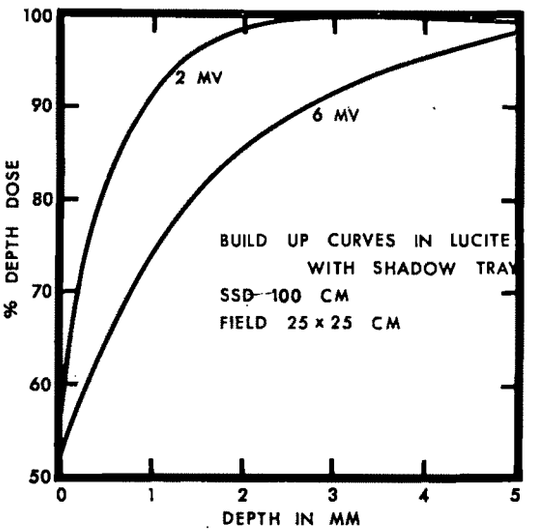


FIG. 9. Comparison of build-up curves for 2 MV. and 6 MV. x rays in lucite.

DISCUSSION

One practical implication of our results is that if a plastic shadow tray is used on a 6 MV. machine, it ought to be attached in place only when treatment calls for the use of lead shielding blocks, and not left thereon all the time. As noted above, this can save a patient's skin from as large as 48 per cent increase in the local dose. For treatments which do need a shadow tray, superficial doses may be further reduced by using a tray made of wire mesh instead of solid plastic. Alternatively, some type of electron filter may be incorporated under it. For the filter, the most commonly recommended material is a metal of middle atomic number, such as tin or cadmium,[3,7] although lead appears to be adequate. The use of leaded glass for shadow trays has been recommended for cobalt 60, but we did not investigate it.[6] Of course, surface doses may be reduced by treating patients at greater distances from a shadow tray, but only if the lower dose rate is acceptable.

From the clinical point of view, it must be remembered that figures like the 48 per cent above concern only the central axis dose and the outermost keratinized layer of skin. As one proceeds inwards into the skin, the corresponding increase in local dose becomes somewhat less, but still can be considerable. For example, at a depth of 0.5 mm., the percentage increase in local dose due to the shadow tray is about 10 to 30 per cent, depending on the size of the field. If the total applied dose were about 2,000 rads, the increase in dose at this depth would be of the order of 200 rads over and above an unavoidable 800 rads. This is generally in the subcutaneous layer of the skin containing blood vessels largely responsible for erythema. This layer extends below a depth of 1 mm., where the increase in local dose can still be as high as 20 per cent. Figures like these must be kept in mind when planning a course of treatment for patients who may be susceptible to acute skin reactions.

SUMMARY

Using LiF powder, the surface dose and build-up were measured in a lucite phantom for several kinds of megavoltage radiation, with the purpose of determining the extent of electron contamination from plastic shadow trays.

For the 6 MV. unit, a shadow tray at 29 cm. from the phantom caused considerable contamination of the beam, leading to an increase in surface dose of up to approx-

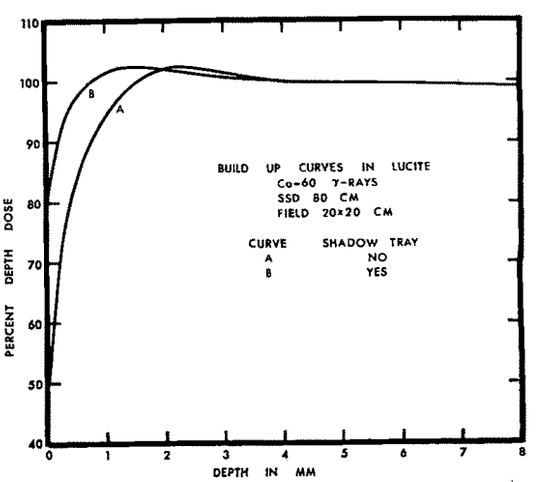


FIG. 10. Build-up curves for cobalt 60 gamma rays in lucite phantom.

imately 48 per cent of local dose for large fields. To eliminate this, different kinds of shadow trays were tried, as well as a lead filter under the tray. The last was found to be most efficient.

For the 2 MV. unit an inherently good geometry led to low electron contamination, while for the cobalt 60 unit poor geometry led to high contamination.

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A NEW METHOD OF ALIGNING A LIGHT LOCALIZER-X-RAY BEAM*

By EARL VAN ROOSENBEEK
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THE field defining illuminator used on x-ray machines, teletherapy units, or high energy accelerators must closely outline the area which the x-ray or electron beam exposes. During initial installation, the light bulb must be moved to align the light beam with the x-ray beam. Once it is satisfactorily aligned, it should be checked periodically to ensure proper patient treatment or examination.

One method of alignment, in use for many years, is to shine the light field onto a cassette-containing film. The edges of the light field are marked with some dense object such as lead; an exposure is made and the film is processed. On a new machine, and frequently when replacing light bulbs on older equipment, the 2 fields will rarely coincide. Some estimate of necessary bulb movement must then be made. The bulb is moved the estimated amount, and another film is exposed. With luck, 3 or 4 films will give satisfactory alignment. More than an hour of adjusting and re-exposing film is common.

Polaroid film packs can be used to hasten the developing process, but they lack the other benefits of the method to be described here.

A better approach has been suggested by Feldman.[2] With this method, the film can be returned exactly to the position it was in initially after it is processed, and the light can be moved to coincide with the darkened area of the film.

A much simpler and more economic method is now available in the form of light- and x-ray sensitive paper. This paper, Kodak linograph 1895, has been suggested by the Bureau of Radiological Health[1] as a faster, more economical method of visualizing x-ray beams.

However, the methods suggested do not take advantage of some of the more important benefits of the Kodak paper. The paper does not need to be used in a film cassette. It can be removed from a light-proof storage envelope or box at the time of exposure in a dimly lit room. Background light can be as high as 1–2 foot candles. The paper can be taped to a fixed surface in the beam path and an exposure made with the x-ray beam. After exposure, the room lights can be turned on. If they are fluorescent lights, the paper will begin to self-process immediately. If the room lights are not fluorescent or not bright enough, a fluorescent desk lamp can be positioned near the paper. Processing of the illustrations used here occurred in less than 1 minute under fluorescent light of 150–250 foot candles.

Since the paper has not been moved in this procedure, the light bulb can now be moved to correspond to the x-ray darkened area.

A verification record can then be made using another sheet of the paper. The light localizer is turned on during some part or all of the exposure, and 2 effects will be observed: the light localizer will expose the paper sufficiently so that the light field can be observed as a lighter area, and the x-ray beam will cause a darkened area. If both fields are the same size, the x-ray penumbral exposure will produce a darkened area slightly larger than the light beam. When the light beam is not properly aligned, the asymmetry of light to dark edges is apparent. A much greater accuracy of alignment is possible than can be obtained using lead markers and trying to approximate the position of the edge of the light beam. An example of this is shown in Figure 1.

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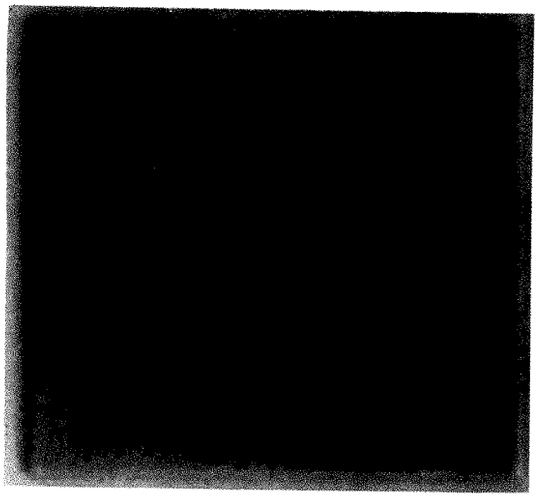


FIG. 1. A 25 mev. photon exposure. Light bulb requires adjustment towards the right side.

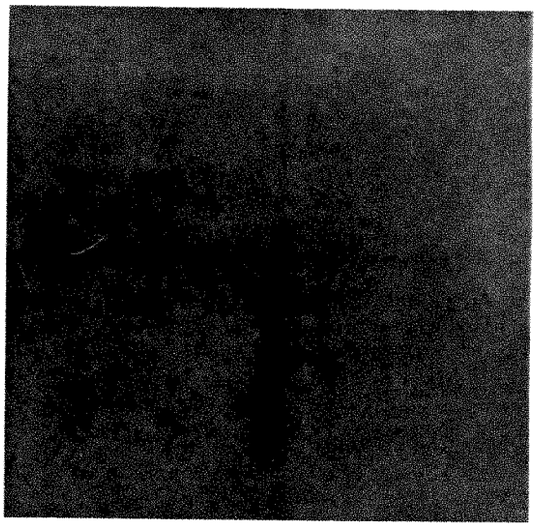


FIG. 3. Same exposure as Figure 2 with light localizer turned on for $\frac{1}{2}$ second before exposure.

Cross hair alignment and light-distance indicators can be displayed simultaneously when present and if desired. This also records the fact that the cross hairs and distance indicator are correctly set, assuming the distance to the paper was first correctly measured using another method, such as a mechanical pointer.

Except with low energy x rays, the paper should be covered during x-ray exposure with sufficient tissue-equivalent material to produce build-up.

The paper will become lighter or darker as 2 opposite effects are occurring—a light-

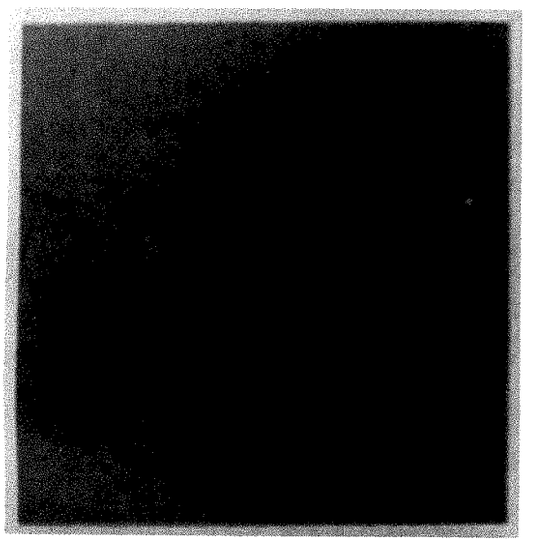


FIG. 2. X-ray exposure on Kodak paper without light localizer on.

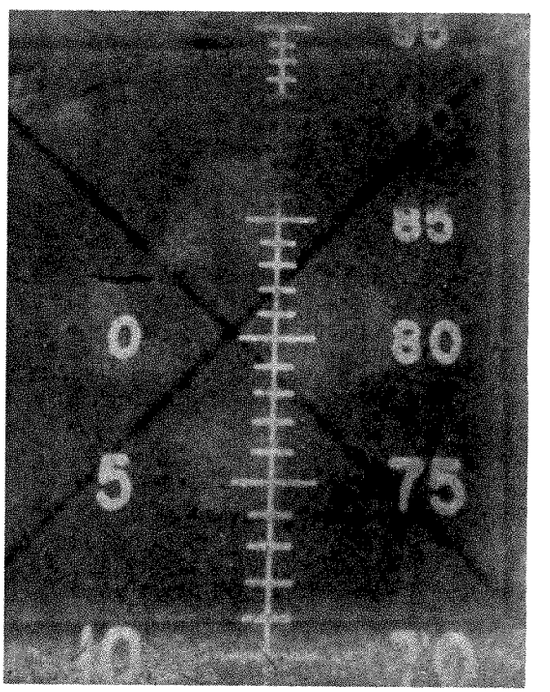


FIG. 4. Theratron 80 exposure showing light beam to x-ray beam conformity and cross hair optical distance indicator alignment.

ening caused by the longer wavelength of light and a darkening caused by the x rays. Some combination of light beam time to x-ray exposure time must be derived in cases where the light beam is very intense. In the illustration of Figure 1, a 25 mev. photon beam exposure of 250 r and a light beam time of 10 seconds was used.

Figure 2 is an exposure made without the light beam; 100 kv., 100 ma., 2 seconds, 50 cm. target-film distance, and 2 mm. Al HVL were used. Figure 3 is the same exposure with the light localizer on prior to x-ray exposure for about one-half second. The light pattern appears exactly as seen by the eye during set-up.

Figure 4 is an exposure made with an A.E.C.L. Theratron 80.* The output of the machine was 125 r/minute at 80 cm., and a 2 minute exposure was made. The light localizer and distance indicator were left on during the exposure.

The paper, which comes in an 8 inch roll 100 feet long, can be cut into convenient 8 inch lengths. This is adequate for a 15 cm. $\times$15 cm. field. Fading of the paper can be prevented by keeping the paper between the pages of the machine log book or by covering with yellow report covers.[1]

SUMMARY

Kodak linograph paper, type 1895, has been found to exhibit a response to both light and x rays in a manner which can be very useful in displaying light beam-x-ray alignment. The paper is insensitive enough to be handled in a low light level room, but self-develops under strong fluorescent light. When a sheet of the paper is attached under an x-ray portal, both the light localizer pattern and the x-ray beam can be seen without disturbing the position of the paper. Light bulb alignment can be obtained by using 1 sheet of 8 inch$\times$8 inch paper, and by moving the bulb only once. The entire procedure can be done in about 5 minutes with greater accuracy than by previous methods.

The method can also be used to display the alignment of cross hairs and optical distance defining lights as a matter of record. The paper becomes a permanent record if placed between the pages of the machine log book and not exposed constantly to further light.

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UPDATING THE MANCHESTER SYSTEM FOR AFTERLOADING*

By W. P. SCOTT, M.D.†
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SEVERAL years ago we developed an Alignment Applicator which combined the best features of the loose system (fitting the ovoids and tandem to conform to the pelvic anatomy) and the rigid system (stable alignment of the ovoids and tandem). This Alignment Applicator[3–7] ensured:

1. Optimal alignment, by having the tandem and ovoids perpendicular to one another which tended to project the uterus cephalad and equidistant between the rectum and bladder and equidistant between the left and right pelvic walls with minimal, if any, deviation.

2. Optimal position, by having the axes of the tandem sources perpendicular to the ovoid sources which in turn were perpendicular to the bladder and rectum (minimal radiation) and parallel to the cervical os (maximum radiation). Consequently, there was no need to correct for "hot" and "cold" spots with external radiation. Furthermore, I believe that the good geometry of a fixed tandem-ovoid system is preferable to the bad geometry of the Heyman capsule system in irradiating the corpus uteri.

3. Optimal fit, by selecting the correct size from the 6 dummy ovoids and 3 tandem lengths. Even the narrowest of fornices and shortest of canals, *e.g.*, stump, would accept the smallest ovoid and single segment tandem.

4. Optimal stability, by converting the loose system to a rigid system. Several patients were inadvertently transported in wheel chairs, and a few were even ambulatory, yet without the slightest change in position of the system noted on roentgenograms. The amount of vaginal hardware was reduced to a minimum, with only a 3 inch $\times \frac{1}{8}$ inch pin remaining in the lower vagina requiring minimal packing.

5. Acceptance of any type of radioactive source in the ovoids regardless of size, shape or number. Furthermore, any type of tandem was adaptable to the Alignment Applicator.

6. Minimal application time of 2 minutes or less using a preloading technique.

However, even this relatively short application time has been criticized in this era of afterloading and, therefore, in order to retain these 6 advantages of the Alignment Applicator, we have modified the ovoids for afterloading. As there are already enough cervical applicators available, we see no reason to design another. We therefore limited the presentation to a modified ovoid of the Manchester type which can be used with any standard afterloading tandem and which will accept any standard radioactive source. Consequently, this device (Fig. 1, *A* and *B*; and 2, *A* and *B*) should interest those therapists who have a large investment in radioactive sources of various sizes and shapes on hand and prefer:

A Manchester type system[2]
A perpendicular rather than a parallel relationship of ovoid and tandem sources (Fig. 3, *A* and *B*)
Vertical elevation of the uterus with minimal if any deviation or flexion
Minimal vaginal hardware
Little, if any, packing
An ideal position of sources and alignment of applicator
Optimal fit of ovoids and tandem to the anatomy[1]
Easy dose calculations due to consistently good geometry (Table 1)

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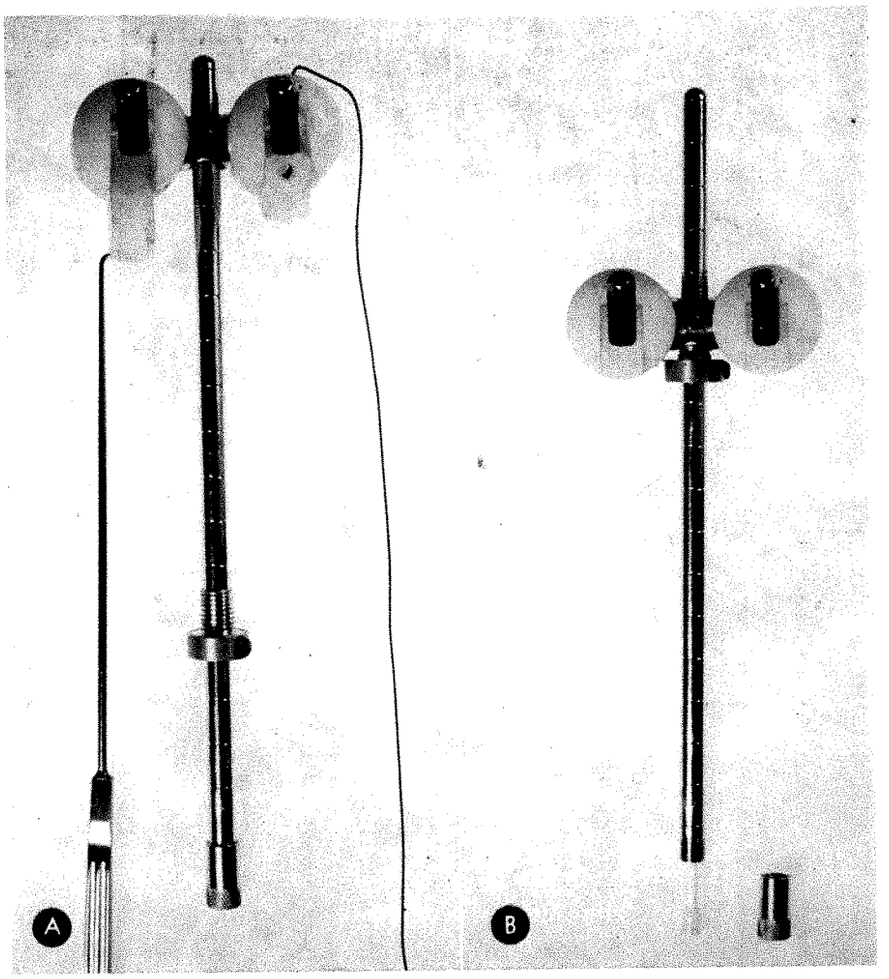


FIG. 1. (*A*) Unassembled system showing how recesses are opened (or closed) with a tenaculum and closed with a suture line. The tandem is passed through the hole in the crossbar after the correct uterine length is preset with a collar which secures tandem to ovoids prior to loading. (*B*) Assembled system showing tandem engaging closed ovoids which will be opened and loaded. Later tandem is tube-loaded at bedside.

A choice of direct or indirect (tube) loading

Rapid and simple application and removal of both applicator and sources.

DESCRIPTION

The basic series of 6 modified Manchester ovoids with a hole in the crossbar as used with the Alignment Applicator are further modified as follows:

A recess is cut out of the ovoid and the resulting block contains a channel to accommodate the radioactive sources. This recess is hinged at its base in order for it to be opened, with the channel changing 90° from a vertical to horizontal position for afterloading. A small clip at the top of the ovoid closes the channel and locks the recess. These channels are drilled large enough to accommodate any size sources or tubes. Either direct loading with long forceps or indirect loading with nylon tubes is possible, but tubes might be preferred, since simple retraction of the tube opens the recess and empties the channel. The tube also allows bedside afterloading along with the tandem. (The same type tube and stylet used to hold and retain the radioactive sources in the tandem serves to afterload the ovoids.) A small transverse

hole set in the face of the recess allows it to be easily opened and closed with a tenaculum. In addition, a hole passing through the back of the ovoid and on into the back of the recess and channel allows closure of the recess with a suture which is preferred to the tenaculum for bedside afterloading. Furthermore, the suture facilitates removal of the ovoid from the vagina.

After the tandem is passed into the uterine canal to determine the correct length, a collar is slipped on and attached

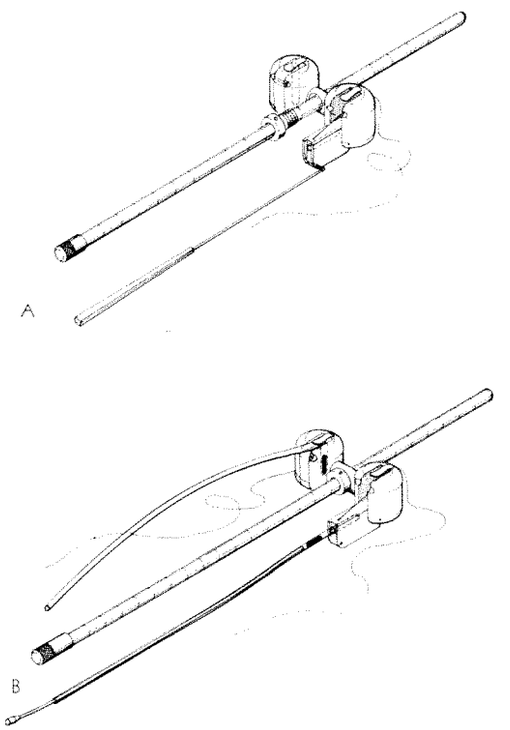


FIG. 2. (*A*) Tandem and adjustable collar for presetting tandem length shown passing through the crossbar of ovoids. For afterloading in the operating room, the recess is opened with a tenaculum and closed with either the tenaculum or a suture line (note the holes provided for these). The tandem is afterloaded at the bedside. (*B*) Assembled system for afterloading (lower ovoid) at bedside. The stylet is removed after the source is deposited and the channel is closed with a suture line to lock and seal the sources within the tube (upper ovoid). Withdrawing the tube opens the channel and removes the source. The same type of tube is used for both tandem and ovoids.

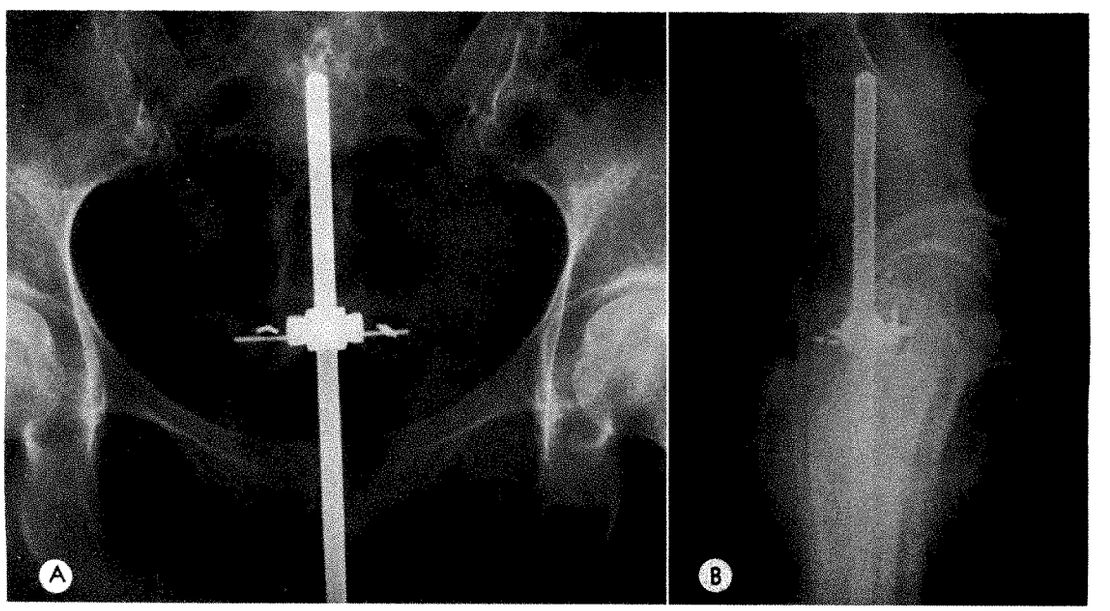


FIG. 3. (*A* and *B*) Roentgenograms of medium ovoids (with spacer) and a 3 segment tandem showing vertical position of the tandem and perpendicular anteroposterior relationship of the sources within the ovoids. (*A*) The anteroposterior roentgenogram shows the transverse pins (hinges) below the sources. (*B*) The lateral roentgenogram shows a clip identifying the anterior cervical lip.

TABLE I

DOSE RATE IN RADS/HOUR TO CONVENTIONAL PELVIC POINTS

20 mg. loading in each ovoid 10 mg. loading in each tandem segment	Filtration = 1 mm. Pt			Filtration = 0.5 mm. Pt		
	Point A	Point B	Cervix	Point A	Point B	Cervix
Large ovoids with spacer	16.3	8.28	52.4	17.4	8.86	56.1
Large ovoids without spacer	16.6	8.00	69.5	17.8	8.56	74.3
Medium ovoids with spacer	18.5	9.20	70.8	19.8	9.84	76.1
Medium ovoids without spacer	19.0	8.50	97.4	20.3	9.10	105.
Small ovoids with spacer	22.3	9.20	133.	23.9	9.84	143.
Small ovoids without spacer	22.1	8.76	160.	23.6	9.37	173.
10	14.5	2.62	33.3	15.8	2.82	36.6
10	12.2	2.53	4.62	13.4	2.73	5.55
10	3.90	1.80	1.33	4.40	1.91	1.72
10	1.80	1.18	0.50	2.10	1.27	0.60

Above factors are for radium and cesium 137. For cobalt 60: 1 mc = 1.56 mg. radium.

with a set screw. The tandem is then passed through the central hole of the crossbar (and on into the uterus) until the threads of the collar engage the threads of this hole. Thus the tandem is easily attached to and detached from the ovoids by merely screwing the tandem in and out.

LOADING

After the tandem and ovoids are introduced and joined, the recesses are opened with a tenaculum, loaded, and closed with either a tenaculum or suture. The channels may be loaded directly with radioactive sources or indirectly with nylon tubes through which sources are then or later transferred by a stylet which is withdrawn before the recess is closed with either a tenaculum or suture. Unloading is easily accomplished by withdrawing the nylon inner tubes from the tandem and ovoids. If the recess has been directly loaded, then the ovoids are pulled out of the vagina by the suture and emptied.

SUMMARY

Universal afterloading Manchester ovoids for use with any standard afterloading tandem and most standard radioactive sources have been designed to:

1. Provide optimal stability, position and alignment with mechanical simplicity.
2. Provide optimum anatomic fit requiring little, if any, packing.
3. Provide rapid application and removal.
4. Eliminate excessive vaginal hardware.

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EXPERIENCE WITH CALIFORNIUM 252 IN CLINICAL RADIOTHERAPY*

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THE use of externally applied fast neutrons in the treatment of cancer has been considered for some time, and a clinical trial is underway.[1,5,9,20] Recently, fast neutron emitting californium 252 (Cf^{252}) sources for interstitial and intracavitary use have been made available by the Atomic Energy Commission for evaluation in the treatment of human cancers. An amount of 229 micrograms of this material was supplied to the University of Texas M. D. Anderson Hospital and Tumor Institute at Houston, Texas in 1968. Preliminary physical,[15,25] radiobiologic[3,7,10–12] and health physics data[16,17,19] have been accumulated by us and others preparatory to the clinical use of these sources.

The rationale for the use of fast neutrons in clinical radiotherapy has been succinctly stated by Brennan and others.[1,2,6] High LET* radiations partially overcome the radiation resistance of anoxic tumor cells which may be present in tumors, the proportion depending upon the size and vascularity of the tumor. The ratio of radiation dose required to affect anoxic cells compared to that required for the same effect in well oxygenated cells is called the oxygen enhancement ratio (OER). The presumed advantage of a fast neutron emitting source such as Cf^{252} depends on its lowering of the OER, estimated to be about 1.6 to 1.7[12] for Cf^{252} compared with about 2.0 for Ra^{226} utilized at clinical interstitial dose rates (30–70 rads/hr.). Therefore a small but possibly important advantage may be gained by using Cf^{252} instead of Ra^{226} or Ir^{192}.

* Linear Energy Transfer: ionization density in kev./micron of path.

Whether or not this theoretic advantage will be demonstrable clinically will ultimately require a controlled clinical trial. Preparatory to this, we have utilized Cf^{252} in a pilot study since November 1969 to evaluate: (1) basic dosimetry and health physics data; (2) workable afterloading techniques; (3) dose specification and computer dosimetry methods; and (4) a clinical impression as to tumor and normal tissue reactions and a clinically useful RBE factor for the neutron portion of the radiation dose.

This report details our experience to date.

PHYSICS

Under a contract with the US AEC (effective on October 15, 1968), 54 sources totaling 229 micrograms of Cf^{252} were loaned to the M. D. Anderson Hospital (Table 1). The initial studies were of pertinent physical and dosimetric measurements. A computer procedure for calculation of neutron dose distribution around an implant was derived to aid in treatment planning.

The relative activities of the afterloading cells were measured either in a National Physical Laboratory Chamber (combined beta-gamma reference ionization chamber, NBS Handbook No. 80) or a BF_3 counter. These relative activities of the short afterloading cells agreed within ± 4.7 per cent, and those of the long afterloading cells within ± 2.5 per cent.

The uniformity of linear activity of the sources was evaluated with autoradiographic techniques to check for spotted lengths, hot ends and cold ends.

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TABLE I

Cf^{252} SOURCES RECEIVED

Type	No.	Active Length (cm.)	Cf^{252} Content (μg.)
Afterloading Cell	18	1.5	0.75
Afterloading Cell	24	3.0	1.5
Applicator Tube	12	1.5	10–20

DOSIMETRY

The gamma ratio and neutron perpendicular bisector dose rates and the neutron-to-gamma ratio of some Cf^{252} sources were determined to a depth of 7.0 cm. in tissue equivalent solution using dosimetry systems similar to those described by Oliver and Wright.[16]

Isodose contours for gamma rays and for neutrons emitted from a Cf^{252} needle were measured in tissue equivalent solution. The gamma dose is depressed at the ends of the needle by the internal sealing plugs; the fast neutron dose rate distribution exhibits no such end effect. As expected, the gamma dose rate (normalized per microgram) from an afterloading cell was higher than that from an applicator tube, because the tube wall (0.7 mm.) is thicker than the cell wall (0.25 mm.). The active length of a source did not noticeably affect the dose rate.

COMPUTER DOSIMETRY

The Department of Biomathematics at the Anderson Hospital has combined into their existing RADCOMP computer program a ninth-order polynomial fit of the calculated results of neutron kerma rate as a function of depth in tissue. This new program CALRAD is based on the same general principles of patient data acquisition from roentgenograms, of multiple line source summations for total physical dose

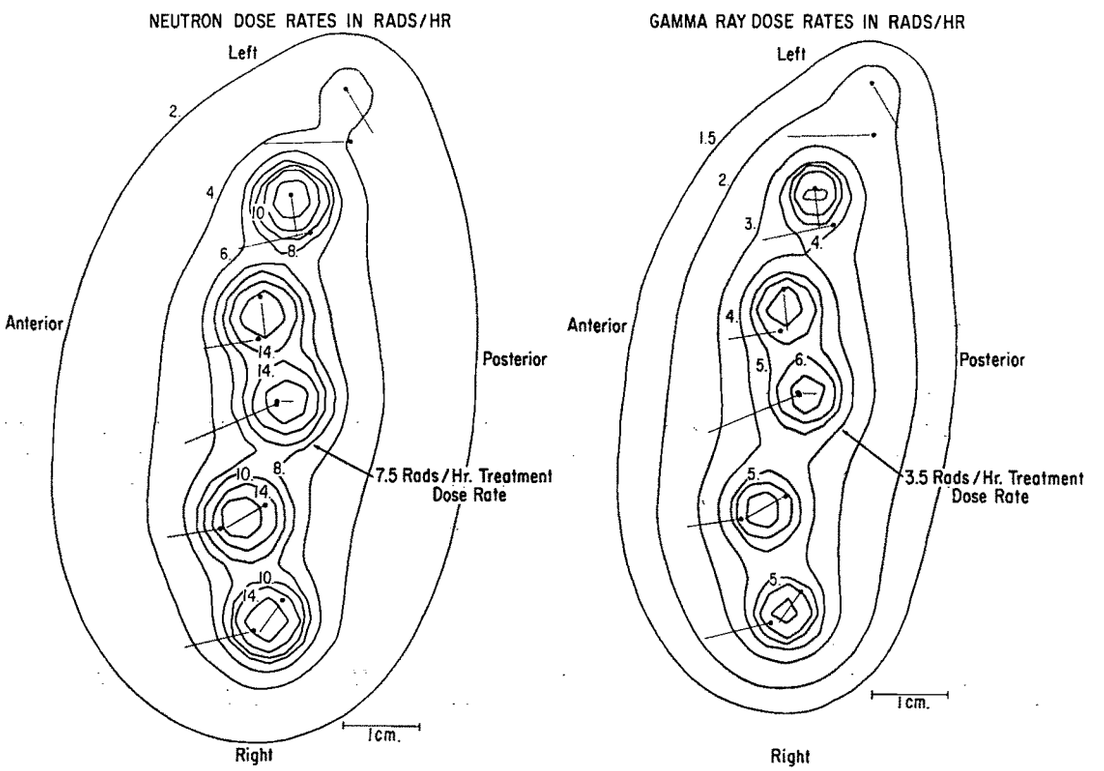


FIG. 1. Case 1 (Table II). Isodose curves for neutron and gamma ray doses about a planar implant. The doses are in rads/hour and must be multiplied by appropriate RBE values (7.0 for neutrons, 1.0 for gamma rays).

estimates, and of plotted and/or listed dose distributions in selected planes (Fig. 1). Gamma-ray and neutron doses are calculable with CALRAD. The salient features of this program are:

A variety of source types can be used—needles, cells, or tubes—as long as such dimensions as active length, physical length, filter thickness, and activity are given.

Multiple isodose distributions can be obtained from planes of calculation having any orientation around or passing through some or all of the sources in the implant.

Input data, derived from roentgenograms, either stereo or orthogonal sets, of the actual implant supply the clinical information required for the computation.

Output data consist of:

a. A tabular listing of dose rates on grid points in the plane.
b. Plotted and labeled isodose curves for both neutron and gamma-ray physical dose rates plus source projections on the plane of calculation.

This calculational method assumes the Cf^{252} sources to be in an infinite homogeneous medium and restricts the use for sources which are located several neutron mean free paths from boundaries—about 4 cm. Another version of this program is being developed to treat the sources in a finite medium, allowing calculations of neutron dose rates through interfaces or inhomogeneities, such as bone, air or irregular contours.

Experimental evaluation of the effect of the tissue-air interface on the tumor dose is in progress to compare with the calculations. Isodose plots comparing typical californium and radium implants will be prepared.

RADIATION SAFETY

Another area of concern is the neutron dose to hospital personnel caring for patients loaded with Cf^{252}. For nursing, only the necessary procedures of patient care are ordered. For the radiotherapists, afterloading procedures for the implantation are required. All personnel use special shielding when dealing with Cf^{252} radiation. A transport shield is utilized by the physicist, or Cf^{252} curator, who assays and transports only those sources required for the specific implant. The transport shield is made of water-extended-polyesters (WEP) and is designed to carry about 10 micrograms with <20 milliroentgen equivalent man (mrem) per hour at the surface. Concentric rings (2 inches thick) of shielding can be added when larger amounts are needed.

A bedside shield has been developed for use by attendants. Two versions of this shield exist—1 is only wide enough for 1 man; the other is 4 feet long. The curved body of the shield protects the blood-forming organs from neutron dose with a 3 to 4 half-value layer (HVL) thickness of WEP; a "Lucite" head shield protects the eyes with a 2 HVL thickness. The head shield moves on a rail the length of the body. The whole shield can be wheeled into place beside the patient by a nurse. The radiotherapist is only slightly hindered when loading or unloading the implant with sources. Calculations of the neutron doses to the radiotherapist's head region while standing behind the shield (as in Fig. 2) for the time required to afterload and remove the Cf^{252} sources from the patient have been performed. The doses are calculated from dose rate measurements made behind the shield with a 10 inch spherical neutron monitor. Except for 2 patients, the dose averaged 1.1 mrem per microgram of Cf^{252} implanted. With 2 patients, difficulty was experienced in removing the afterloading cells from the guide tubes. The bedside shield was therefore removed to improve access to the patient, and, as a consequence, the therapist received doses 3 times higher than he received during other implant procedures. This emphasizes the desirability of shielding the radiotherapist and the advantage of using uncomplicated afterloading techniques.

For the total 162 micrograms of Cf^{252} implanted, the radiotherapist received an estimated 180 mrem over a period of 1 year.

If Cf^{252} is to be used for treatment of gynecologic cancers, extreme caution must be used because large amounts of Cf^{252} are required. Afterloading devices should be developed, preferably remotely operated. WEP or other high hydrogen content material can be utilized for the neutron shielding. Because the Cf^{252} and Ra^{226} tubes are about the same size, each may be adapted for use in this type of device.

PATIENT EYE LENS DOSE

Of particular concern in these preliminary studies is the dose delivered to the eye lens by implants of lesions in the head and neck region. Several patients had implants ranging from 10 to 15 cm. from one eye lens; a neutron dose to that lens of 0.4 to 60.0 rads was calculated for the treatment period. If an RBE of 15 is assumed, the biologic dose approaches the extrapolated dose to give an observable effect in humans, but not necessarily to produce a vision-impairing defect. One patient (Case 7, Table II) received a very high lens dose because of close proximity of 1 source to the eye.

RADIOBIOLOGIC CONSIDERATIONS IN CALIFORNIUM THERAPY

There is no fixed value for the biologic effectiveness of Cf^{252} emission relative to that from Ra^{226}. The most important variable determining RBE is the dose-rate from Ra^{226}. A less important factor is the changing ratio of neutron to gamma-ray dose from Cf^{252} as the distance from the source increases, the result of a more rapid attenuation of the neutron component in tissue beyond about 0.5 cm. from the source. Since ~40 rads/hr. is a commonly sought dose rate with radium implants, the RBE that we need to use is that for californium neutrons relative to radium gamma rays given at ~40 rads/hr. This RBE value may then be applied to the dose that would be given from Ra^{226} to determine the Cf^{252} neutron dose required.

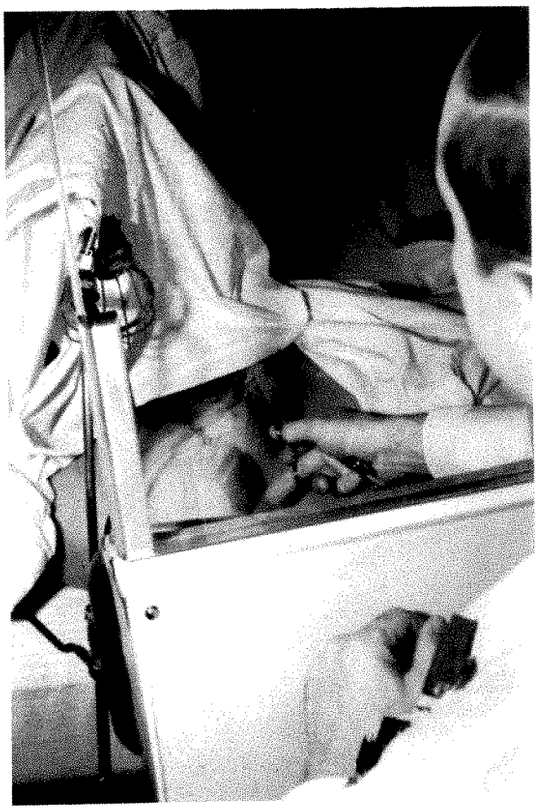


FIG. 2. Afterloading behind californium shield. Note lucite viewing shield equal to 2 HVL for Cf^{252} neutrons.

It should be noted now that a rad of neutrons is several times more effective biologically than is a rad of gamma rays given at low dose rates. Therefore, in considering biologic effects, it is unreasonable to sum physical dose rates of the neutrons and gamma rays emitted by Cf^{252}. The gamma contribution should be reduced to its neutron-equivalence (by dividing by the appropriate RBE value) or ignored altogether,[13,23] since its biologic effect represents less than 10 per cent of the total. RBE values discussed in this section relate to a comparison of Ra^{226} gamma rays and Cf^{252} neutrons only, or Cf^{252} neutrons with a minimal adjustment (8 per cent) for the contribution of Cf^{252} gamma rays.

Our experiments compared the effect of

TABLE II

Case	Tumor	Cf^{252} Dose	External Roentgen Treatment	Results
1	Squamous cell carcinoma of cervix, metastatic to inguinal lymph nodes	6,100 rem 109 hr.		Local control until death at 8½ mo., skin-dry desquamation
2	Squamous cell carcinoma of vagina, Stage IV	2,560 rem 25 hr.	5,000 r	Distant metastasis at 5 mo., local control in pelvis
3	Squamous cell carcinoma of cervix, Stage III, metastatic to inguinal lymph nodes	4,000 rem 100 hr.		Local recurrence at 10 mo.
4	Squamous cell carcinoma of lung, metastatic to right submandibular lymph node (4.5×3.5×2.0 cm.)	2,260 rem 40 hr.		Died 12 days after implantation of cerebral vascular accident, ? distant metastases (brain)
5	Squamous cell carcinoma of vagina, Stage III	970 rem 24 hr.	5,000 r	No evidence of disease at 17 mo.
6	Recurrent squamous cell carcinoma of lower lip (post surgery)	1,920 rem 30 hr.	5,000 r	Local failure at 2 mo.
7	Basal cell carcinoma of right nasolabial fold	4,250 rem		Local recurrence at 5 mo.
8	Squamous cell carcinoma of lung with skin nodules	6,000 rem 70.5 hr.		Died from distant metastases at 6 wk., local lesions much smaller, no moist skin reaction
9	Squamous cell carcinoma of upper lip	2,050 rem 26 hr.	5,000 r	No evidence of disease at 17 mo.
10	Squamous cell carcinoma of vagina	1,250 rem 51 hr.	5,000 r	Local control at 14 mo.
11	Squamous cell carcinoma of vagina, Stage III	1,600 rem 25 hr.	5,000 r +1,000 Parametrial	Local control at 14 mo.
12	Squamous cell carcinoma of cervix, metastatic to distal urethra	2,790 rem 69 hr.	3,000 r Transvaginal	Died 3 wk. later of cerebral vascular accident
13	Recurrent squamous cell carcinoma (lip) in neck (post roentgen-ray treatment)	4,205 rem 66.7 hr.		Died 9 mo. later, regression but persistent tumor
14	Squamous cell carcinoma of tongue T_3N_0 (2nd primary carcinoma)	4,000 rem 70.3 hr.	2,500 r after 3 treatments	Persistent tumor
15	Squamous cell carcinoma of tongue, T_3N_2	2,700 rem 67 hr.	5,500 r	Persistent tumor

Table II *cont.*

Case	Tumor	Cf^{252} Dose	External Roentgen Treatment	Results
16	Metastatic carcinoma to neck lymph node (6×6 cm.)	2,220 rem 44 hr.	6,000 r	Persistent tumor at 3 mo., expired 3½ mo.
17	Squamous cell carcinoma of skin, metastatic to neck lymph node	2,000 rem 21 hr. 1,900 rem 29 hr.	5,000 r	Persistent tumor at 3 mo.
18	Melanoma of cervix and vagina	11,000 rem from mucosal dose, 2 applications		Regression at 4 mo., positive biopsy at 8 mo.
19	Melanoma of vagina	7,500 rem 96 hr.		Local recurrence at 3 mo.

Cf^{252} neutrons and Ra^{226} gamma rays on survival of proliferative cells in the intestinal mucosa of mice.[23] For technical reasons it was impossible to use dose rates of less than 160 rads/hr. from Ra^{226}. Our estimate of RBE (Cf^{252} neutrons only/Ra^{226} gamma rays, 160 rads per hour) was about 5.2, which is similar to the value for pig skin determined by Atkins *et al.*[3,4] using 160 rads/hr. Ra^{226} gamma rays. This is not surprising since the dose-survival characteristics of jejunal crypt cells and skin epithelial cells are similar,[24,25] and there would be little opportunity for regeneration to affect the response of either tissue during the exposure which lasted 24 hours or less. The RBE (Cf^{252} neutrons/Ra^{226}) value is about 7, when the Ra^{226} dose rate to pig skin is reduced to 35 rads/hr.[23] We have assumed, therefore, that this value would also be relevant to killing of cells of the intestinal mucosa, when dose rates of 35 rads/hr. from Ra^{226} and 5 rads/hr. from Cf^{252} neutrons were used. The RBE value we use now for clinical purposes is 6.5, meaning that 1 rad of Cf^{252} neutrons is 6.5 times as damaging as 1 rad of gamma rays given at 40 rads per hour.

Although cell killing by Cf^{252} is probably relatively independent of dose rate (except for the minor killing by the gamma component), the effect of regeneration in rapidly proliferating tissues cannot be ignored. Therefore, it is desirable to deliver the treatment with Cf^{252} in about the same over-all treatment time as would be used with Ra^{226}. For example, if a Cf^{252} treatment involving exposure to intestine were given in 7 days, there would be more regeneration of intestinal mucosa during the Ra^{226} treatment. Consequently, the Cf^{252} treatment would be more damaging. In other situations, the proliferation occurring during the few days of treatment is probably of relatively minor significance. Nevertheless, protraction of treatment time may modify tissue response in other ways and if Ra^{226} and Cf^{252} are to be compared in clinical trials, it is desirable that the same over-all treatment times be used. This is an important consideration because most Cf^{252} sources available to date give a *biologic* dose rate higher than that given by conventionally used Ra^{226} sources; hence, over-all treatment times using Cf^{252} have tended to be shorter than for Ra^{226}. Although equal treatment times should be used, it should be noted that unless some rapidly regenerating tissue such as intestine is at risk, no correction need be made to the total

dose prescribed with Cf^{252}, if the dose rate from an implant happens to be greater than the equivalent of 40 rads/hr. from radium. This contrasts with the practice with Ra^{226} and reflects the independence of tissue response and dose rate when Cf^{252} is used.

A further reason for trying to protract the treatment time with californium to equal that with radium is that reoxygenation[15] requires time and, if it is important in determining the response of human tumors, then better responses would be expected from slower treatments.

CLINICAL MATERIAL

From November 1969 to May 1971, 19 patients with either locally far advanced or disseminated neoplasms received either interstitial (17 patients, 18 implants) or intracavitary (2 patients) implants with Cf^{252} as all or a portion of their radiotherapy. Twelve of the 19 patients had some amount of external radiotherapy prior to the implantation. Sixteen of the 19 patients had squamous cell carcinoma, 1 had basal cell carcinoma and 2 had malignant melanoma.

The sites of implantation were mainly metastatic inguinal or cervical lymph nodes or advanced vaginal or intraoral tumors (Table II). Where possible, superficial sites were selected to evaluate the response of overlying skin. Attention was primarily directed to: (1) tumor response; and (2) radiation reaction in normal tissues. Unfortunately, follow-up was often short because of the advanced state of the

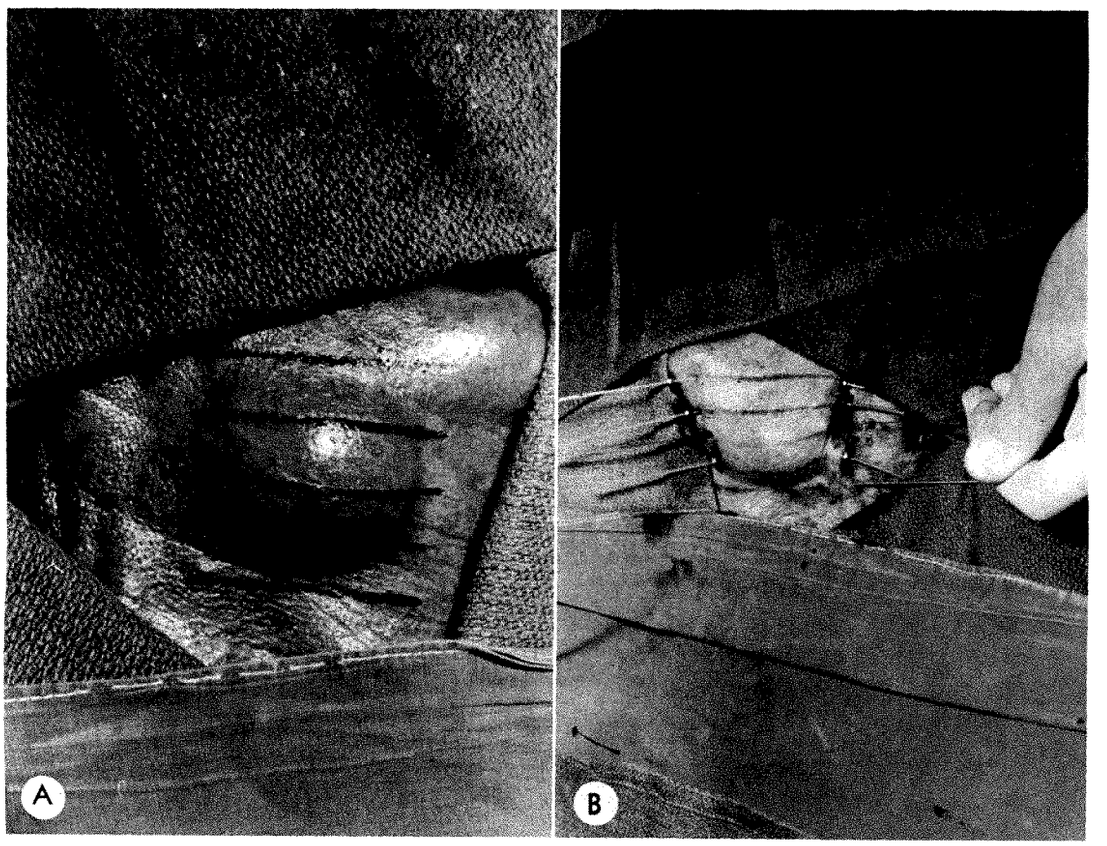


FIG. 3. (*A*) Case 4 (Table II). Skin markings to facilitate percutaneous placements of metal guides. (*B*) Insertion of nylon tubes in operating room. The californium is afterloaded from behind shields after roentgenograms are taken and the patient has returned to room.

disease. The patients were followed to death or local recurrence with frequent observations, the longest follow-up being 17 months.

TECHNIQUES OF IMPLANTATION

An afterloading technique for implantation was developed from that used by Pierquin for Ir^{192} implants.[19] Either solid or flexible metal guides were used to allow percutaneous insertion of nylon or teflon tubes through the tumor which were secured by stainless steel buttons (Fig. 3, *A* and *B*), following which dummy sources were inserted for taking control roentgenograms. These roentgenograms both verified the proper placement of the sources and also provided data input for the computer dosimetry program.

In the case of vaginal implants, hollow stainless steel needles were utilized instead of nylon tubes. For intracavitary implants, a long metal intrauterine tandem which protruded into the vagina was utilized. Plastic vaginal cylinders were fitted over the tandem to maintain the vaginal mucosa at a definite distance. Sources could thus be placed both in the uterus and vagina. Cf^{252} sources may also be fitted into standard afterloading vaginal applicators such as the Fletcher-Suit colpostats.[22]

Thus, in all cases, afterloading of the radioactive sources could be accomplished, reducing personnel exposure significantly. Despite the difficulties in developing convenient techniques for afterloading of intraoral implants because of the diameter (0.95 mm.) and rigidity of the Cf^{252} sources, direct implantation of Cf^{252} needles was rejected as too hazardous because of the neutron exposure to physicians' hands and eyes. Future modifications of Cf^{252} sources to make them more flexible may facilitate such implantations. The desirability of a Cf^{252} wire similar to Ir^{192} wire is obvious for intraoral implants.

The types of interstitial implantations performed included single and double plane as well as volume implants. Anatomic coverage of the tumor volume was considered of primary importance in placement of the sources. The lines of sources were ordinarily separated by 1.0–1.5 cm. The implants were either crossed, where indicated, or extended sufficiently beyond the visible or palpable tumor to obviate the need for crossing. No special distribution rules regarding linear intensity or spacing of sources were utilized. Computer obtained dosimetry was utilized in all cases to specify minimum tumor dose and treatment volume.

REPORT OF CASES

Case 7 (Table II). This 87 year old white male had a basal cell carcinoma of several years' duration arising in the right nasolabial fold and infiltrating the right cheek, upper lip and commissure and extending into the right ala nasi. Central ulceration was present. An extensive surgical procedure was considered too risky in view of his medical condition. A Cf^{252} implantation was performed (Fig. 4) using percutaneously inserted nylon tubes. The implant was left in place for 67 hours, delivering what was thought to be 7,000 rem. A line of sources crossing the center of the implant through the ala nasi was not included in the dose calculation. Later a dosimetry error was found and the dose was recalculated at 4,250 rem at 0.5 cm. distance from the plane of the implant.

An RBE factor of 7.5 was used for the neutron dose. The patient developed a moist epidermitis which healed rapidly with formation of new atopic skin over the ulcer (Fig. 5). Within 5 months, however, there was recurrent disease circumferentially about the ulcer site undoubtedly related to underdosage (Fig. 6).

The dose to the right eye lens was calculated by computer dosimetry to be about 600 rem (RBE 10) because 1 source was placed very close to the eye. This was thought justifiable because of the patient's age and the presence already of bilateral cataracts.

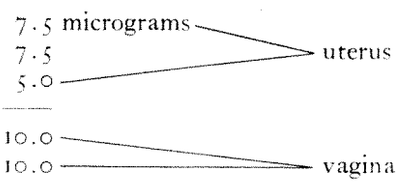
Case 18 (Table II). This 70 year old Negro female presented with vaginal bleeding from malignant melanoma completely infiltrating the cervix and upper vagina. Palpable infiltration was present in both medial parametria. The uterus could be sounded 3 inches, however. The patient had numerous severe medical problems and was not able to withstand radical surgery.



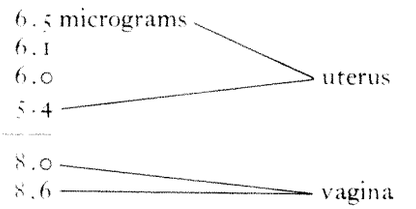
FIG. 4. Case 7 (Table II). Photograph of basal cell carcinoma of the right cheek with percutaneously inserted nylon tubes into which Cf^{252} sources were afterloaded. Later modification utilized larger diameter teflon tubes for outer tubing into which smaller diameter nylon tubes containing the Cf^{252} sources were afterloaded.

Therefore a 72 hour intracavitary Cf^{252} application was performed and repeated 4 weeks later. Sources were afterloaded into a long metal intrauterine tandem which extended into the vagina so that both the uterus and entire length of the vagina were irradiated (Fig. 7, *A* and *B*). Three cm. diameter plastic vaginal cylinders were fitted over the tandem.

Using an RBE of 7.5 for the neutron component of the Cf^{252} dose, computer curves were obtained for various Cf^{252} loadings for the same system (Fig. 8, *A–D*). Cf^{252} loadings were then approximated depending on the available supply of Cf^{252} sources. The desired ratio of milligrams of radium to micrograms of californium appeared to be 1.0: 0.45. A "standard" loading of Cf^{252} for this implant would be:



The following loading was actually used for this patient:



A vaginal mucosal dose of approximately 11,000 rem was given in 2 applications. The total number of microgram hours was 5,165.

An initial regression of tumor was noted at 4 months, but tumor recurrence was present 8 months after treatment. No untoward bladder or rectal effects were noted. An estimation of the maximum dose to rectum and bladder from the computer isodose curves was 7,300 rem in 144 hours.

DISCUSSION

Our preliminary intent was to explore normal tissue reaction and tumor control in locally advanced primary tumors, skin or subcutaneous metastases or metastases to lymph nodes. Oral cavity, neck, groin, skin and vagina were the common anatomic sites. Initially, following the sug-

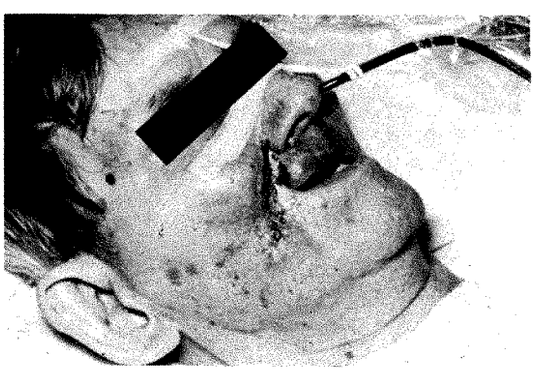


FIG. 5. Case 7 (Table II). Approximately 1 month after implantation moist reaction was apparent in the irradiated area; this healed within 4 weeks.

gestion of Atkins *et al.*,[3] a clinical RBE of 5 was selected for direct comparison of interstitial Cf^{252} implants to Ra^{226} implants, considering the total Cf^{252} dose, both neutron and gamma. Over the expected treatment distances of 0.5 cm. to 1.5 cm. for planar implants, and up to 5 cm. for volume implants, the neutron to gamma ratio for Cf^{252} was expected to be fairly stable.

The selected RBE of 5.0 was soon separated into the following components to give a more logical approach and facilitate computer isodose output:

Neutron dose (rads) × 7.5 (later, 7.0) = neutron dose in rem
Gamma dose (rads) × 1.0 = gamma dose in rem
total dose in rem

Total doses of 6,000–7,000 rem were the objective, where interstitial implantation alone was the therapy. Where external irradiation was utilized in addition to Cf^{252} therapy, the patients often received 5,000 rads in 5 weeks with either Co^{60} teletherapy or 22 mev. photon irradiation followed by 1,500–3,000 rem from Cf^{252}. An attempt was made to utilize similar dose rates as might be obtained with Ra^{226}. In practice, the dose rates with Cf^{252} varied from 25–125 rem/hour, most from 25–60 rem/hour. Dose rate dependence was not expected to be a significant factor with Cf^{252} therapy. No untoward effects were observed with the higher dose rates.

The dose specification for the intracavitary applications was somewhat more complex, since no guidelines were available. Empirical loadings with computer dosimetry gave a ratio of 1.0 mg. of Ra^{226} to 0.45 micrograms of Cf^{252} to produce similar isodose curves surrounding "standard" tandem and colpostat gynecologic loadings when an RBE of 7.5 was utilized for the neutron portion of the Cf^{252} dose.

Since uterine or vaginal tumors may provide suitable sites for californium therapy, it is advisable to develop techniques related to previous experience with radium. Cf^{252} sources can be fitted to afterloading intracavitary applicators, so that standardized loadings will provide known isodose levels around the applicators. Experience with tumor control as well as bladder and rectal tolerance is needed.

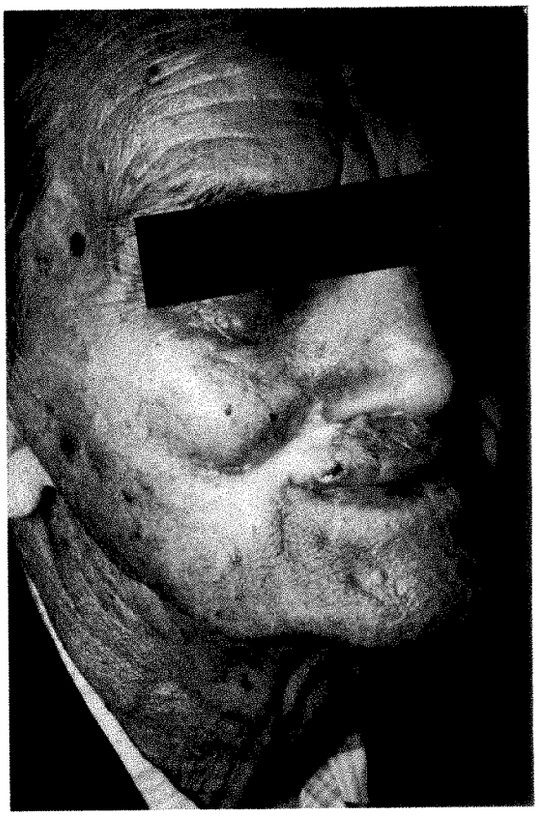


FIG. 6. Case 7 (Table II). At 4½ months after implantation thin atopic skin has covered the ulcer, but there is persistent disease at the edge of the previous ulcerated area: 4,250 rem were delivered instead of the planned 7,000 rem.

Table II shows the local results in the irradiated site. At least 3 of the local failures are believed attributable to underdosage due to dose miscalculation. Excluding these, the rate of local control was encouraging and clinically compatible with the advanced disease. Skin and normal tissue reactions were also within the expected range suggesting that the RBE of 6.5–7.5 for the neutron dose was reasonably correct.

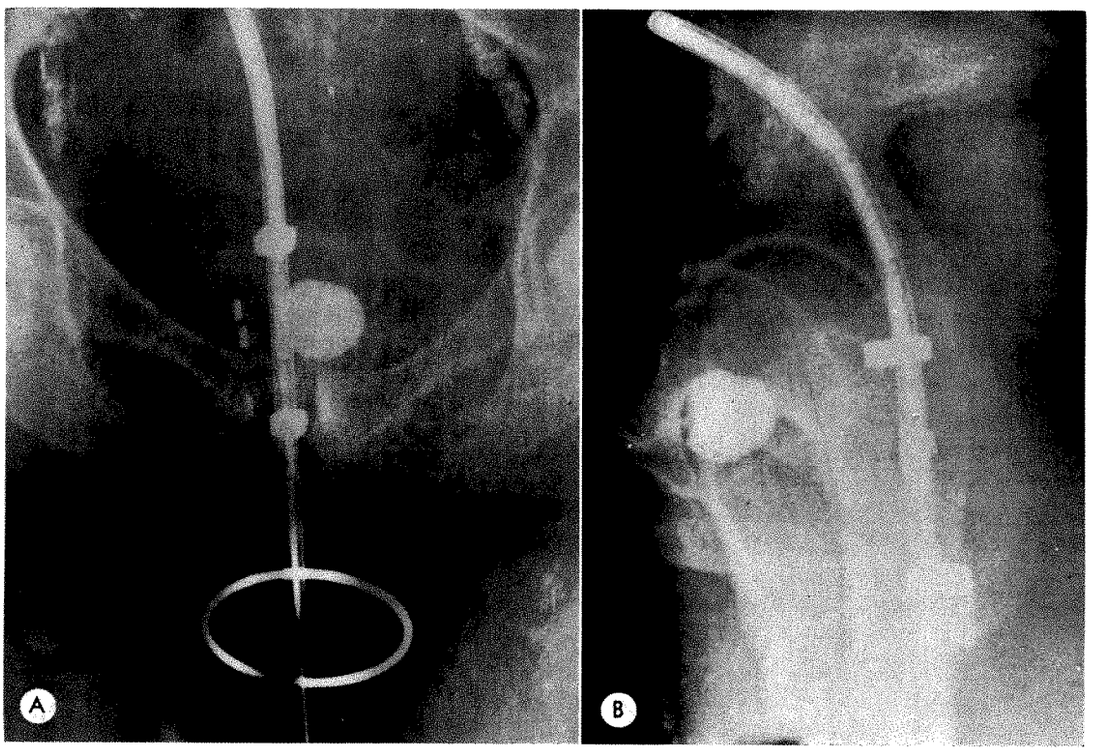


FIG. 7. (*A*) Case 18 (Table II). Anteroposterior roentgenogram of long metal intrauterine and vaginal tandem. Plastic vaginal cylinders hold the mucosa at a specified distance. Dummy sources are loaded for roentgenography. (*B*) Lateral view. Six Cf^{252} sources were afterloaded into the tandem to line the uterine canal and upper 1/2 of the vagina.

Californium may be best utilized as "boost" therapy after a basic dose with gamma ray irradiation in order to control the anoxic central tumor or it may be of value alone in certain tumor sites. Techniques and tumor sites for a prospective randomized clinical trial are needed in order to adequately answer the question of its relative efficacy to gamma emitting isotopes.

CONCLUSIONS

1. Afterloading techniques are required to maintain a low exposure dose to personnel and assure a reasonably geometric implant with Cf^{252}.

2. The clinical impression of 6.5–7.0 for the neutron RBE for Cf^{252} appears correct.

3. A number of patients with advanced disease have had local control of the tumor indicating that Cf^{252} is an effective interstitial source.

4. Intracavitary use of Cf^{252} is feasible and may be the easiest to standardize. A ratio of 0.45 micrograms of Cf^{252} to 1.0 mg. of Ra^{226} is suggested for gynecologic implants.

5. Increased precautions and care must be taken in handling Cf^{252} and patients to prevent overexposure of health personnel; this must be weighed in assessing the usefulness of Cf^{252}.

6. Decay of Cf^{252} may be a problem in maintaining a sufficient amount of the required intensities, especially for gynecologic implants. A bank may be needed to replenish sources fairly frequently.

7. A controlled clinical trial will be needed to prove or disprove the greater

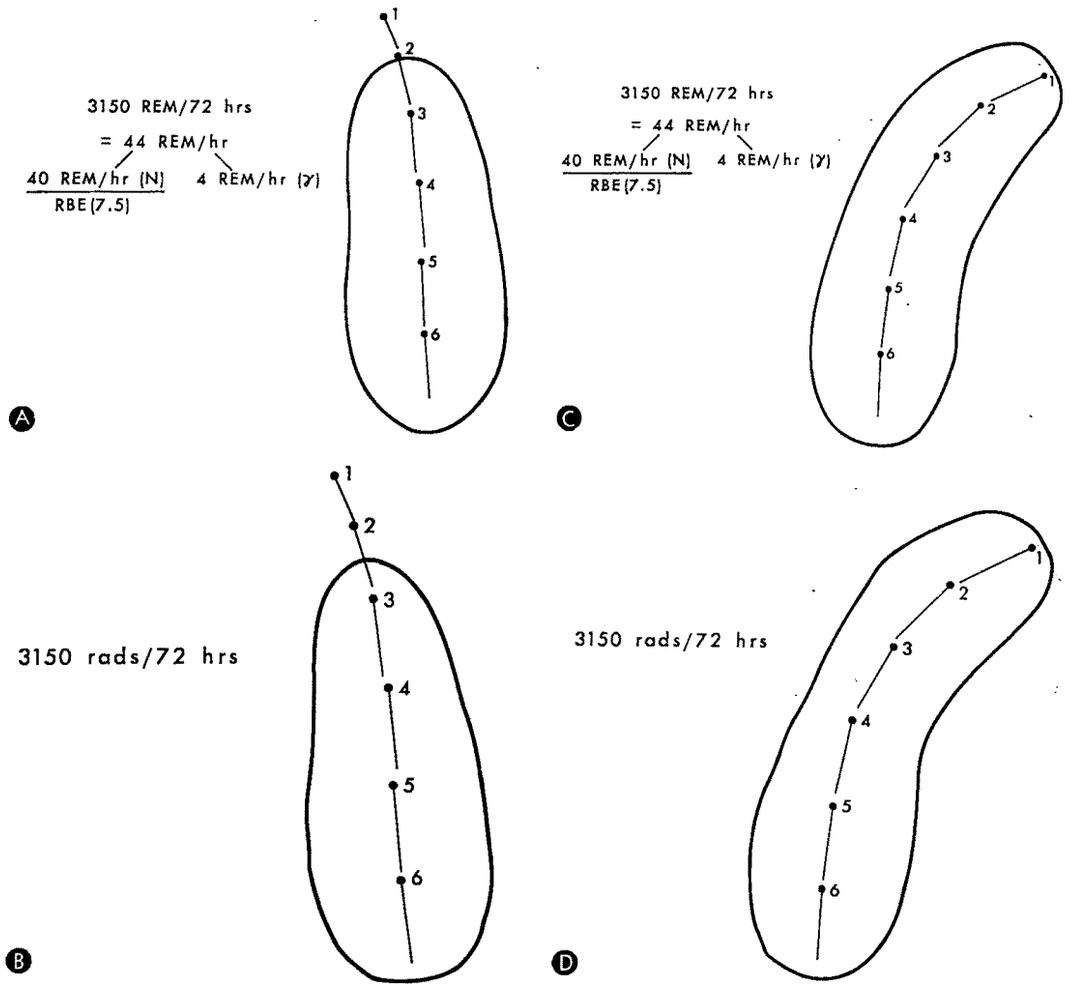


FIG. 8. (*A*) Case 18 (Table II). Californium loading. Computer obtained isodose curve (heavy black line) outlining tumor volume receiving a minimum of 3,150 rem in 72 hours. Sources: 1—6.5; 2—6.1; 3—6.0; 4—5.4; 5—8.0; 6—8.6 micrograms.

(*B*) Standard radium loading. Similar isodose curve for 3,150 rads in 72 hours. Sources: 1—15; 2—15; 3—10; 4—10; 5—20; 6—20 milligrams. Note similarity of isodose curve shape and area with ratio 1 mg. Ra to 0.45 μg. Cf.

(*C*) Lateral view of same californium isodose curve, as in *A*.

(*D*) Lateral view of same radium isodose curve, as in *B*.

effectiveness of Cf^{252} over that of gamma emitting sources such as Ra^{226} or Ir^{192}.

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A COMPARISON OF TECHNETIUM 99M AND IODINE 123 FOR THYROID IMAGING*

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THYROID imaging is commonly performed with iodine 131 and technetium 99m with a few individuals also using iodine 125. Certain limitations are inherent in the use of each of these radionuclides. In consideration of the "ideal" radionuclide for thyroid imaging, iodine 123 has been mentioned as possessing many of the characteristics which would make it most suitable for the purpose.[2,5] Unfortunately, it has not been readily available, and, where it has been used, problems of contamination with iodine 124 have seriously impaired its effectiveness.

Recent developments have suggested that iodine 123 may yet achieve the status in thyroid imaging that its physical and biologic characteristics indicate it should occupy. The cyclotron production of Xe^{123} by the Te^{122} (He^4, 3N) Xe^{123} reaction with decay of Xe^{123} ($T_{\frac{1}{2}} = 2.1$ hr.) to I^{123}($T_{\frac{1}{2}} = 13.3$ hr.) has resulted in "carrier-free" iodine 123 of high radionuclidic purity,[3,7] where 0.2 per cent I^{125} is present at delivery and no I^{124} is present. The production of millicurie quantities of high purity iodine 123 has been demonstrated[3] using these reactions in combination with rigorous purification of Xe^{123}. The possibility of large-scale production of iodine 123 by large accelerators such as at Brookhaven National Laboratory (BLIP), Los Alamos (LAMPF) and Vancouver (TRIUMF) may mean ready availability at very reasonable cost.

It seemed useful, therefore, to look again at the clinical utilization of iodine 123, now available in pure form. Since it has a similar photon energy to that of technetium 99m and, as with technetium 99m, is conveniently used with the gamma camera, we decided to carry out a comparison of the 2 nuclides for thyroid imaging with the gamma camera equipped with a pin-hole collimator.

METHOD

It was necessary, in this study, to operate within the constraints imposed by the use of technetium 99m. Larger amounts of iodine 123 had to be used and the iodine study had to be performed at a time greater than about 15 hours to avoid interference by technetium in the iodine study.

Patients were first examined with technetium 99m pertechnetate ($Tc^{99m}O_4^-$). Approximately 2.5–3.0 millicuries were administered intravenously and images obtained on the gamma camera at 30 minutes after administration. The distance from the pin-hole of the collimator to the anterior surface of the extended neck was 6 cm. Fifty thousand to 100,000 counts were collected in 3–10 minutes.

After completion of technetium imaging, iodine 123 as NaI^{123} was administered orally. The dose was usually 100 to 350 microcuries, although in a few instances images were obtained after only 60–75 microcuries. The patient returned in 18 hours for uptake measurement and scintiphotography. Using the same distance we usually obtained the same number of total counts with iodine 123 as with technetium 99m when possible, but in a number of instances this was not feasible.

The images were then evaluated by 2 observers as to significant features and were rated as either excellent, fair or poor. The final thyroid status of each patient was determined by consideration of uptake data, serum T_4, clinical status and other

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TABLE I

DIAGNOSIS IN 100 PATIENTS EXAMINED WITH Tc^{99m} AND I^{123}

Hypothyroid	5
Euthyroid	77
Hyperthyroid	15
Subacute thyroiditis	1
Chronic thyroiditis	2

tests such as serum-free thyroxine, TSH, thyroid autoantibodies, etc., where indicated.

RESULTS

There were 102 examinations performed on 100 patients. Two patients had repeat studies following attempted suppression with triiodothyronine. The distribution of patients according to diagnosis is listed in Table I.

In evaluation of the diagnostic quality of each examination, it was evident that in the vast majority of cases both radionuclides were excellent agents for imaging (Table II). However, the background contributed substantially to the image in the technetium scintiphotos and detracted from the sharpness of detail. It also necessitated accumulation of more counts with Tc^{99m} than with I^{123} for equal information over the thyroid. Approximately 95 per cent of the counts accumulated in the I^{123} image were in the thyroid, whereas only 40–50 per cent of the counts were from the thyroid in the Tc^{99m} image.

TABLE II

COMPARISON OF Tc^{99m} AND I^{123} FOR THYROID IMAGING IN 102 EXAMINATIONS (100 Patients)

	Excellent		Fair		Poor	
	Tc^{99m}	I^{123}	Tc^{99m}	I^{123}	Tc^{99m}	I^{123}
Hypothyroid	1	1	2	3	2	1
Euthyroid	66	78	10	0	2	0
Hyperthyroid	15	15	1	1	0	0
Subacute thyroiditis	0	0	0	1	1	0
Chronic thyroiditis	1	2	1	0	0	0
Total	83	96	14	5	5	1

The difference in the number of excellent images obtained with the 2 radionuclides in favor of iodine 123 is statistically significant ($P \sim 0.005$) by the chi-square test. This is not surprising in view of the better target-nontarget ratio with iodine. It is more apparent when reviewing some images. In several instances nonfunctioning nodules were clearly seen on the radioiodine image but were barely perceptible with technetium (Fig. 1, *A* and *B*; and 2, *A* and *B*). In 8 instances the pyramidal lobe was noted on the iodine study, but not with techne-

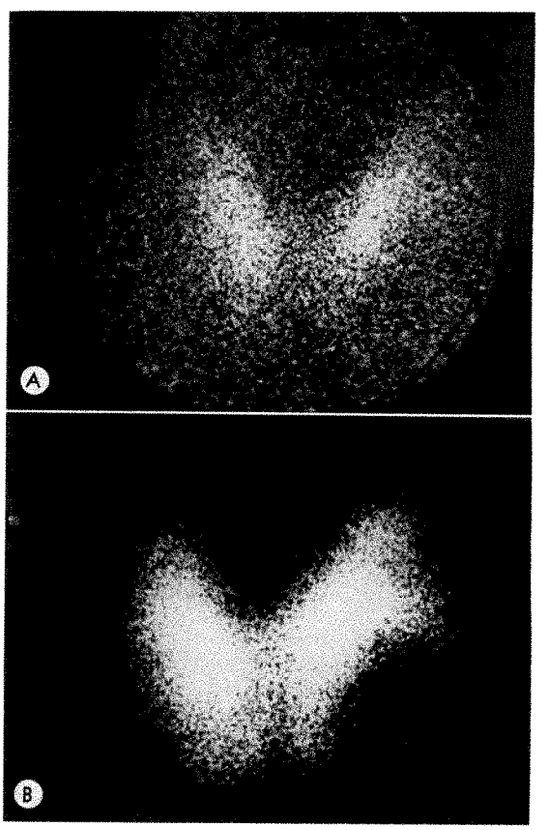


FIG. 1. Euthyroid woman with palpable nodule in lower pole of left lobe. (*A*) $Tc^{99m}O_4^-$ (0.49%). The nonfunctioning region is not visualized with any degree of certainty, but is well shown in (*B*) the I^{123-} (19.5%) image. The Tc^{99m} uptake is rather low. (The numbers in parentheses indicate per cent uptake.)

tium, probably due to the high level of background activity (Fig. 3, *A* and *B*). In 1 instance this was due to improper positioning. The technetium study showed a pyramidal lobe not seen with radioiodine in only one instance.

Discordant results were noted in 5 other patients. One patient with a large substernal goiter had a poorly defined gland as seen with Tc^{99m}. The borders were so indistinct that substernal extension could not be ascertained, but a single functioning nodule could be seen at the left upper pole. The radioiodine study clearly delineated a substernal goiter with multiple functioning nodules (Fig. 4, *A* and *B*). Another patient

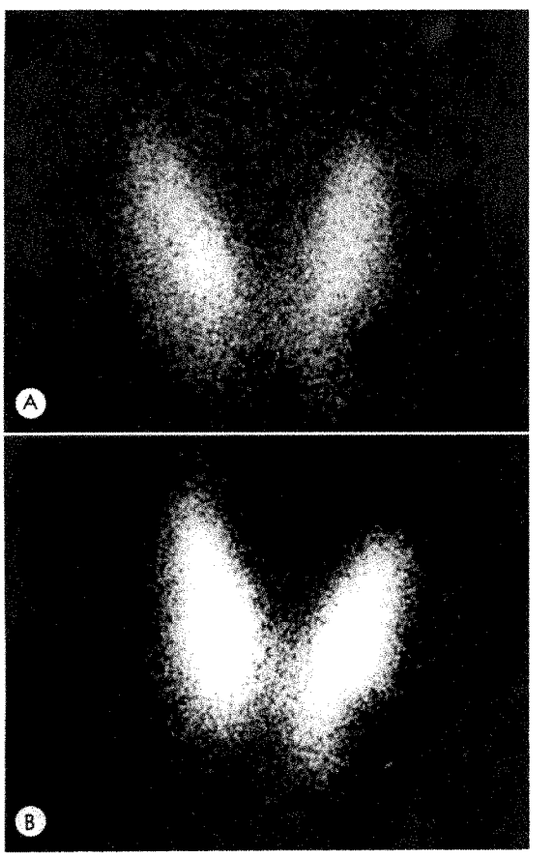


Fig. 2. The barely perceptible nonfunctioning nodule in (*A*) the $Tc^{99m}O_4^-$ (1.37%) image, is clearly visible in (*B*) the I^{123-} (23.5%) image, in the lower pole of the left lobe. Poor delineation in the Tc^{99m} image is noted despite good uptake and fairly low background.

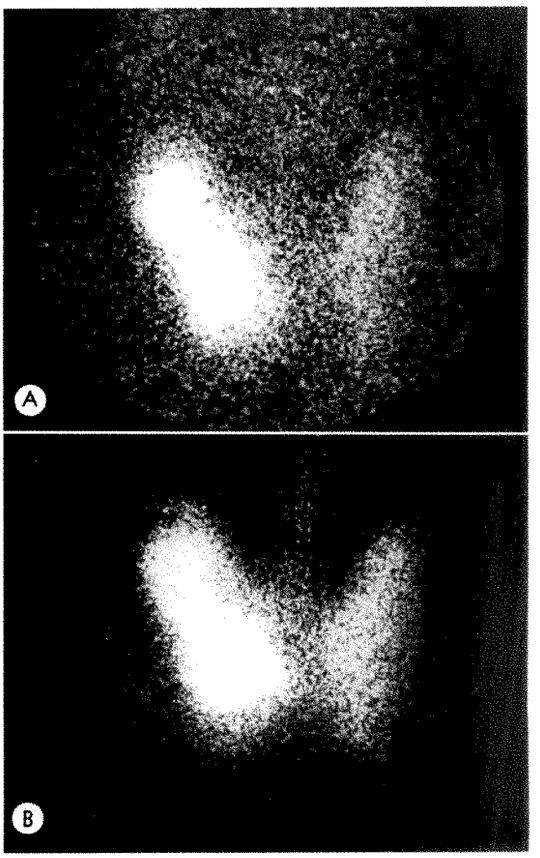
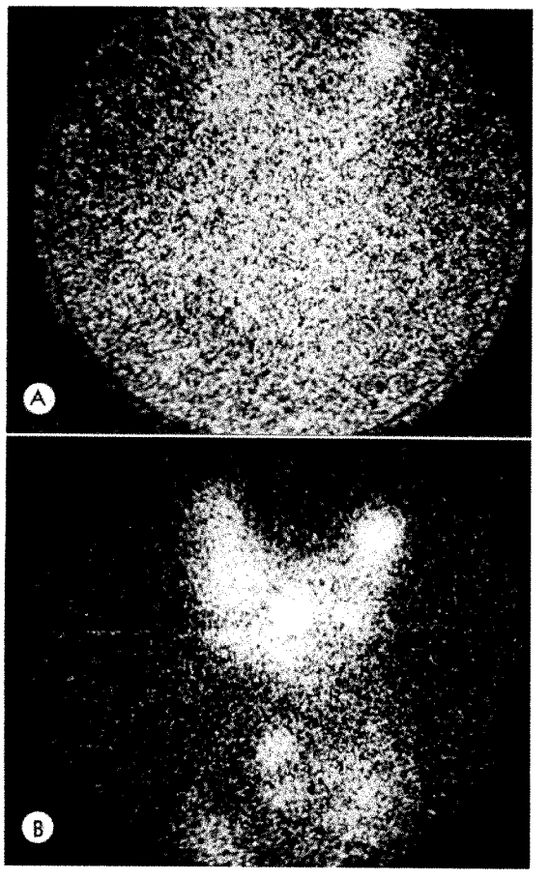


Fig. 3. The right lobe is irregular and somewhat enlarged. (*A*) $Tc^{99m}O_4^-$ (1.91%). (*B*) I^{123-} (29.1%). A pyramidal lobe can be identified in the I^{123} image, but is lost in the background activity with Tc^{99m}.

with Hashimoto's thyroiditis had an enlarged gland which was nodular to palpation, but not clearly so on the technetium study. The radioiodine examination demonstrated multiple functioning nodules (Fig. 5, *A* and *B*).

Of special interest are 3 patients with functioning nodules on the technetium examination which were either non- or normally functioning on the iodine study. One of these patients had had radioiodine treatment for hyperthyroidism 18 months before, the other 2 were euthyroid (Fig. 6, *A* and *B*; 7, *A* and *B*; and 8, *A* and *B*). The significance of these differences is not known.

In a number of patients the technetium



scintiphoto displayed what was apparently an inferior extension (Fig. 9, *A* and *B*). This was not seen in the iodine image, nor in other views of serial, sequential, Tc^{99m} scintiphotos taken over the 30 minutes immediately following injection in many of these patients. We have assumed this to be coating of the pharynx with saliva containing Tc^{99m}. It has been noted by others.

A summary of the anatomic findings noted in this series is seen in Table III.

DISCUSSION

Previous studies[5,9] have been hampered by contamination of I^{123} with I^{124}. Not only does this increase patient radiation dose, but images are degraded by collimator

FIG. 4. This patient had over-all normal function, although the uptake values were low. (*A*) The $Tc^{99m}O_4^-$ image shows a very indistinct outline of the thyroid and a single functioning nodule in the upper pole of the left lobe. The I^{123-} (10.5%) image shows a well defined thyroid outline with multiple functioning nodules and a rounded substernal extension containing several functioning nodules.

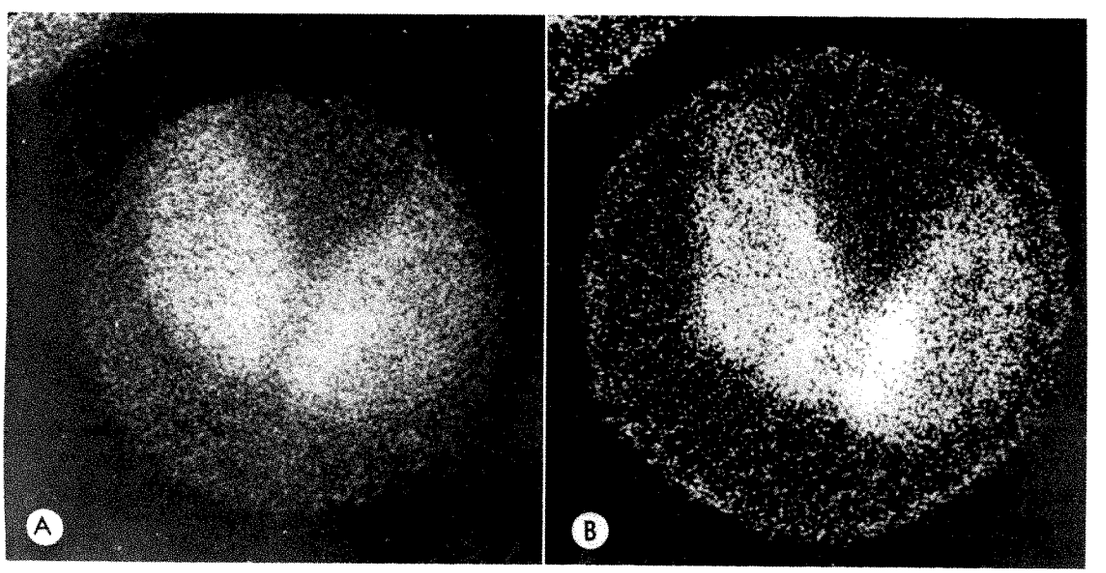


FIG. 5. A male patient with an enlarged thyroid for at least 2 years had a thyroid autoantibody titer of 1:2,500,000 (normal up to 1:25), normal uptake values and circulating hormone levels. (*A*) $Tc^{99m}O_4^-$ (3.02%) image shows enlargement and irregularity of radioactivity distribution, but the several functioning nodules can only be appreciated on the I^{123-} (21.8%) study.

TABLE III

FINDINGS IN THYROID IMAGES OF 100 PATIENTS

	Tc^{99m}	I^{123}
Nonfunctioning nodule	8	9
Functioning nodule*	10	7
Multiple nodules	16	18
Substernal goiter	0	1
Pyramidal lobe†	30	37

* In 1 patient, a single functioning nodule was seen on Tc^{99m} image, multiple nodules on I^{123} image.

† One patient was poorly positioned to view pyramidal lobe on Tc^{99m} image. In 1 patient the pyramidal lobe was seen with Tc^{99m}, but not with I^{123}.

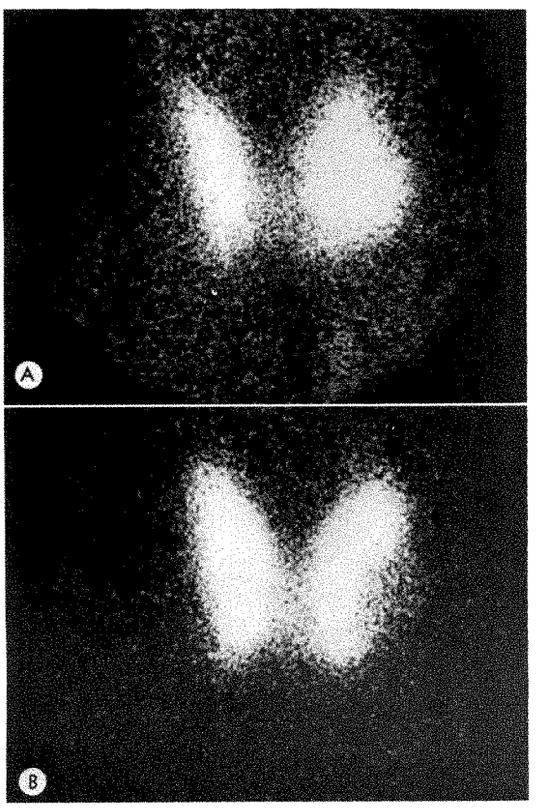


FIG. 6. Pertechnetate and I^{123} images in a woman who had received a therapeutic dose of I^{131} for hyperthyroidism 18 months before this study. At the time these images were obtained she was euthyroid with a palpable nodule in the left lobe. This nodule is noted to be functioning on the (*A*) $Tc^{99m}O_4^-$ 30 minute study, but nonfunctioning on the (*B*) I^{123-} 18 hour study.

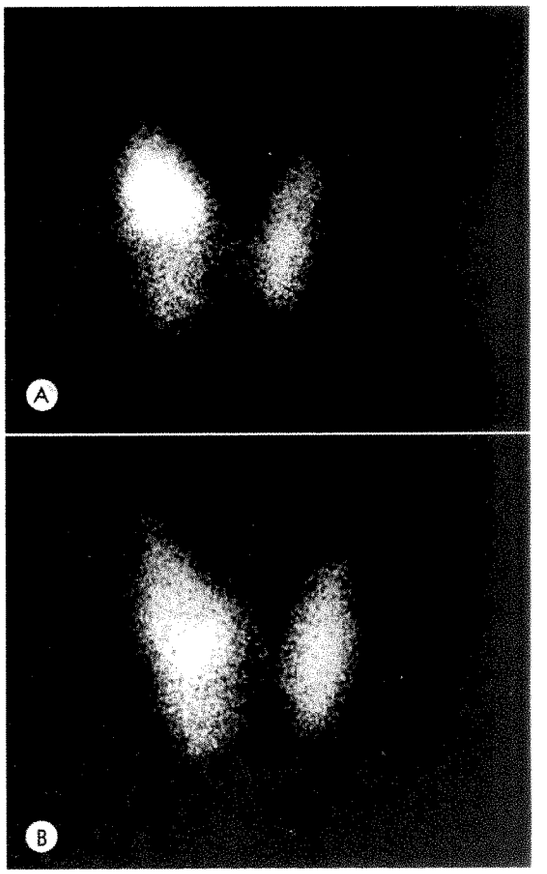


FIG. 7. This woman was euthyroid but with a Tc^{99m} uptake at the upper range of normal. A palpable thickening of the right lobe is seen to be functioning to a greater extent than the rest of the gland with (*A*) $Tc^{99m}O_4^-$ (3.50%) study, but is about equal in function to the remainder of the gland with (*B*) I^{123-} (22.6%) study.

septal penetration and by scattering of the 602 kev. and 722 kev. gamma photons of I^{124}. This contamination becomes worse if studies are done at 24 hours or with I^{123} which has been allowed to stand for some time, because of the longer half life of I^{124} (4.1 days) compared to I^{123} (13.3 hours).

A comparison of I^{123} with I^{131} would not be expected to yield any evidence of great superiority of I^{123} over I^{131}, particularly when using the rectilinear scanner, other than that due to the ability to use larger quantities of activity without excessive radiation dose. The radiation dose from I^{131} is 50–100 rads/μc. When using a

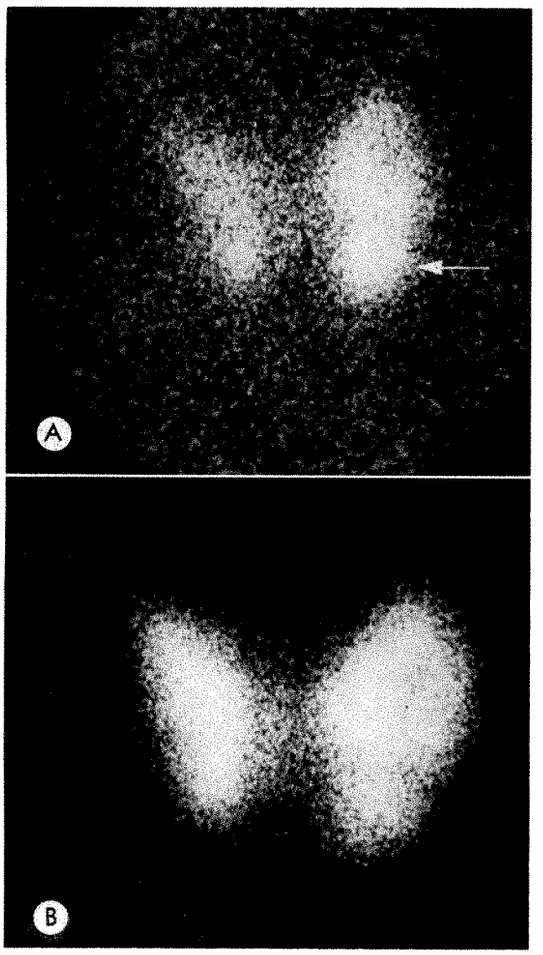


FIG. 8. This patient had a palpable nodule in the left lower pole for at least 6 years. There had been no recent change. (*A*) $Tc^{99m}O_4^-$ (1.16%) study shows, in addition to a widened upper pole, a functioning area (arrow) in the lower pole on the left. This is not apparent on the (*B*) I^{123-} (17.3%) study.

gamma camera there is a definite advantage to the use of I^{123} because of the better efficiency of detection by the thin crystal for the 159 kev. gamma photon. A further advantage is gained by the low efficiency of detection of the 1.3 per cent gamma emissions at 530 kev. of I^{123} which are not useful for imaging.

One disadvantage of using the gamma camera is the inability to utilize the 27.5 kev. x-ray emission associated with Te^{123}.

A more interesting comparison is that of Tc^{99m} and I^{123}. Both radionuclides contribute about the same radiation dose to the thyroid for their usual administered activities (0.7 rad/2.5 mc Tc^{99m} and 1.0 rad/100 μc I^{123}) and have similar principal gamma photon energies for use with the gamma camera. Because of the much higher concentration of I^{123} in the thyroid, a much lower total body radiation dose is encountered compared to technetium. The much higher target-nontarget ratio for about the same number of microcuries in the thyroid at the time of administration for I^{123} results in a superior image of the gland.

The use of technetium 99m in this comparative study caused some deviation from

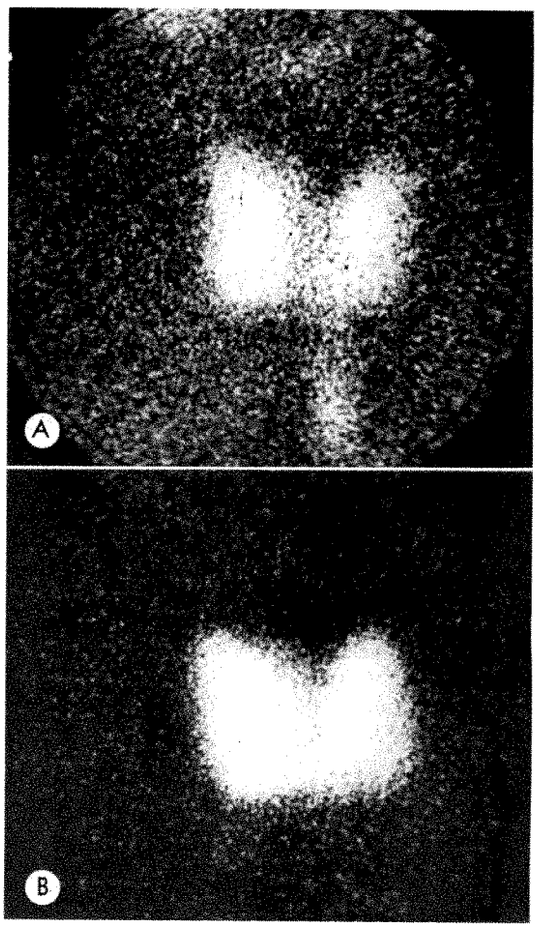


FIG. 9. An apparent extension from the inferior portion of the gland is noted on (*A*) the $Tc^{99m}O_4^-$ (1.41%) study, but not on the I^{123-} (30.6%) image. It is presumed to be saliva containing Tc^{99m} coating the upper esophagus.

optimum utilization of I^{123}. Due to residual Tc^{99m} at 18 hours with a similar photon energy, the I^{123} administered activity had to be larger than otherwise necessary. This is particularly true because 6 hour uptake and imaging would have made it possible to reduce the amount of I^{123} administered by two-thirds to achieve about the same results.

Of special interest are those patients in whom there was a discordance between the images found by the trapping phase with Tc^{99m} and those illustrating the organic binding phase with I^{123}. These discrepancies have been noted by others,[1,4,8] and have been attributed to various factors such as localized binding deficits or carcinoma. We have no definite explanation for our cases. Because of the difficulty in obtaining histologic material on most patients referred for thyroid imaging, it may be some time before it will be possible to categorize these thyroids. Hopefully, with further experience, a better understanding of these situations will be possible.

CONCLUSION

Iodine 123 is a nearly "ideal" radionuclide for thyroid imaging.

An efficiently collimated and detected photon emission combined with a short half life allows relatively large amounts of activity to be used with low radiation dose.

It can be utilized with the gamma camera and produces superior images to those obtained with Tc^{99m} because of its greater concentration in the thyroid with a consequent reduction in background counts.

Some discrepancies in images with I^{123} and Tc^{99m} have been found which cannot be explained at this time.

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ILLUSTRATION OF ISODOSE CURVES WITH THE APPLICATION OF THE SABATTIER EFFECT*

By FRANCISCO ALANÍZ-CAMINO, M.D., *and* DAVID ESPEJO, B.S.
MONTERREY, MÉXICO

IT HAS been recognized that intracavitary irradiation is essential in the treatment of carcinoma of the uterine cervix. Since the beginning of the present century[3] many applicators have been used to irradiate the uterus and vagina and later several afterloading techniques have been described.[1,4] Some of the techniques involve the use of remote control[5,11] and linear distribution of the sources.[6,8]

In our Hospital we have adopted an afterloading linear applicator: the source of radiation is cesium 137.

It is the purpose of this report to present a qualitative illustration of the distribution of radiation around the applicator using the photographic phenomenon of solarization.

MATERIAL

The applicator consists of a plastic tube with a curvature of 20°, and graduated each centimeter on the exterior surface. This tube is inserted into the cervico-uterine cavity after it has been expanded to accommodate a No. 8-9 Hegar dilator. A plastic ring with 2 metallic markers is used as a reference at the external os. A plastic applicator consisting of 2 cylinders with a lead shield oriented to shield the rectum and the bladder is then inserted into the vagina. With this applicator there is little need for extra packing. The plastic tube is large enough to protrude through the vulva. The whole system is supported by means of a lucite perineal bar which has 2 holes to allow for a Foley catheter and the plastic tube; the bar is in turn secured to an abdominal belt (Fig. 1).

METHOD

A wax phantom was constructed with the applicator located at its center. In this position it was possible to simulate the distribution of radiation within a patient. An industrial radiographic film was irradiated in the phantom. This film was placed in proximity to the applicator on the plane where we wanted to know the distribution of the radiation. It was then irradiated using different source loadings during an irradiation time sufficient to have a good darkening; call this the film "patron."

The film "patron," after developing, was placed in contact with an unexposed film, and the combination was exposed to a luminous source of 40 watts at a 50 cm. distance for a relatively long time, depending on the transparent curve we wanted (15–900 sec.). The second film was developed partially (one-half of the total time) and then was exposed totally to the same source of light for a shorter time (5 sec.). The film was developed completely and fixed and washed.

In this manner we obtained a family of transparent curves that were related to regions of isodensity. This set of curves was exposed in successive steps onto a third radiographic film, and this film was developed to produce reproductions as shown in Figures 2 to 5.

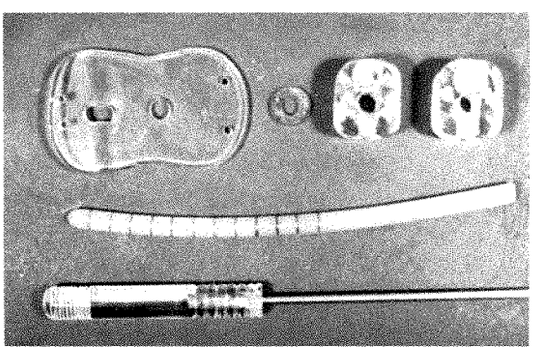


FIG. 1.

* From the Department of Radiation Therapy, Hospital San José de Monterrey, Monterrey N.L., México.

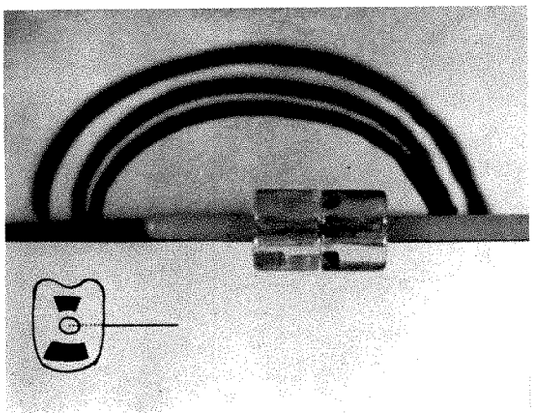


Fig. 2.

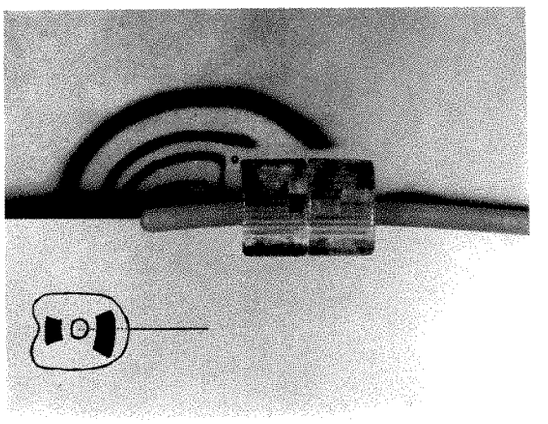


Fig. 4.

This technique has been described in detail in other publications.[2,7,9,10]

RESULTS

With the phenomenon of solarization under the basic conditions of interaction of radiation with matter, it is possible to visualize the radiation distribution of several cesium 137 sources localized in a cervico-uterine applicator.

Figure 2 shows the distribution of a linear arrangement of 15+15+15+15 mg. radium equivalent of cesium 137. The plane is longitudinal and passes between the 2 lead shields.

Figure 3 shows the distribution of a linear arrangement unequally loaded with a heavy source in one end, 10+10+10 +10+50 mg. radium equivalent of cesium 137.

Figure 4 shows the effect of the shielding in a longitudinal plane. The lead shield is 12 mm. thick and is incorporated into the posterior half of the vaginal cylinders to protect the rectum.

Figure 5 shows the effect of shielding in a transverse plane. The source of radiation was 50 mg. radium equivalent of cesium 137.

CONCLUSIONS AND SUMMARY

We were interested, during the construction and dosimetry of a cervico-uterine applicator, in the graphic form of the distribution of radiation on several planes around the applicator itself.

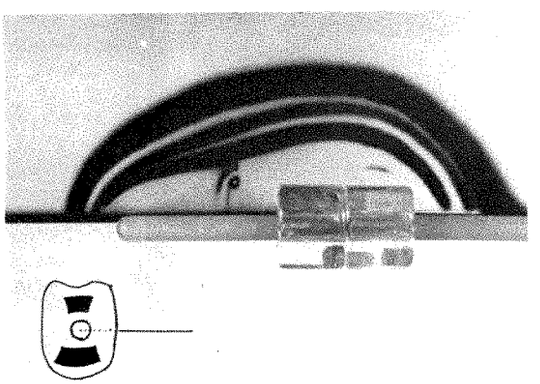


Fig. 3.

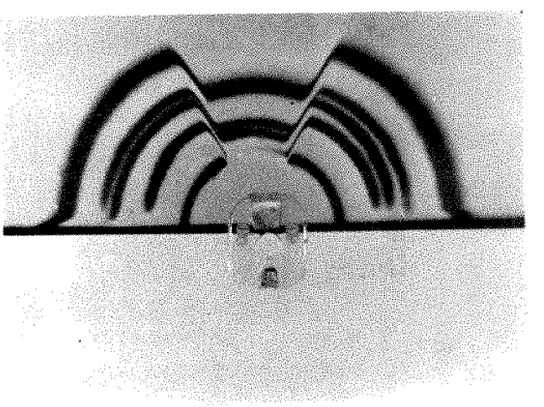


Fig. 5.

The method used to visualize this distribution was carried out with the very useful photographic phenomenon of solarization, better known as the Sabattier effect.

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Fifty-fifth Annual Meeting: Broadmoor Hotel, Colorado Springs, Colorado, April 22–26, 1973.

EDITORIAL

FIFTY-FIFTH ANNUAL MEETING OF THE AMERICAN RADIUM SOCIETY

THE 55th Annual Meeting of the American Radium Society will be held at the Broadmoor Hotel in Colorado Springs from 22 to 26 April 1973. The last time the Society met there was in 1961. A return engagement was booked at the request of many members who recall the exceptionally satisfactory presentation of the scientific program made possible by the superbly equipped auditorium facilities of the Broadmoor and its trained professional staff.

Probably, they are also remembering the warm hospitality of this resort, with its atmosphere of western living, the rugged beauty of the surrounding Colorado mountains, the sunshine and the clear, blue, smog-free skies. The hotel has added new meeting rooms and ultramodern convention facilities. The pools, gardens, courts, links, trails, theaters, lounges, shops and other facilities for recreation and entertainment are constantly being made better. Geographically, Colorado Springs is more convenient for the majority of our members than are most other meeting sites of comparable attraction.

The Scientific Program, which appears in detail elsewhere in this issue, has been designed to present a balance of subjects. Radium and its successors are not neglected. In addition, it was recognized that the membership has evolved to a constituency of oncologists, each of whom has a field of special competence. The largest categories are therapeutic radiologists, gynecologists, head and neck surgeons, and other surgical specialists. Physicists are a numerically small contingent of vital importance, and the Society is strengthened by the presence of internists, pathologists and others concerned with the goal common to the group. The topics of the papers for this meeting were chosen with attention to all of these interests.

On Monday a gynecologic symposium, organized by Dr. George C. Lewis, Jr., will expose for discussion the current controversies in coping with the lymphatic spread of pelvic cancer. On Tuesday information on developments in the treatment of patients with fast neutrons will be brought up to the minute by the leaders of the major U.S. neutron therapy programs in a symposium chaired by Dr. James T. Brennan. On Wednesday Dr. Philip Rubin will give a progress report on the national cooperative prospective studies in cancer therapy. On Thursday Mr. H. M. Parker will lead an incisive assessment of the hazards of radioactive materials used for treatment and our efforts to control them.

There will be distinguished Guest Lecturers from abroad. Professor Brigit van der Werf-Messing, Director of the Radiotherapy Institute in Rotterdam, Netherlands, will report on experience in the treatment of prostatic cancer. At another time she will review the treatment of bladder cancer. These sessions will provide opportunities for discussion of new findings reported at the Conference on Genitourinary Cancer, which the American Cancer Society has scheduled for Washington in March. Mr. Ronald W. Raven, Consulting Surgeon at the Royal Marsden Hospital and Cancer Institute and also at the Westminster Hospital, London, who is Chairman of the Marie Curie Memorial Foundation for Cancer and Chairman of the British Association of Surgical Oncologists, will present selected topics on the treatment of head and neck cancer.

The traditional feature of the Meeting is the Janeway Lecture. This year it will be presented by Dr. Juan A. del Regato, distinguished Past President of the Society, friend and teacher of many of the members. Also featured will be the award-winning paper by a resident, selected by a panel of judges under Dr. Jerold P. Green.

More than 20 proffered papers will be presented. These have been selected by the Scientific Program Committee from a much larger number submitted. The choices were most difficult because of the excellence of so many of the abstracts received. However, the principle of balance of subjects was observed. The time for formal presentation was restricted to provide an opportunity for both prepared and spontaneous discussion from the audience.

The working sessions will start early, with business breakfasts at 7:45 A.M. and scientific programs from 9:00 A.M. until 1:00 P.M. Afternoons will then be free for exploration of the indoor and outdoor attractions of the region. Tours are planned of the U.S. Air Force Academy and of the Cripple Creek and Royal Gorge scenic areas. A limited number of registrants who apply in advance may visit the NORAD Defence Center tunneled under Cheyenne Mountain.

Dr. Chahbazian and the Local Arrangements Committee have planned a series of social events, beginning with a reception for arriving guests on Sunday. On Monday evening the Broadmoor's famous Western Show will accompany a ranch-style dinner. Bring your jeans or other western costume if you wish. The Annual Banquet will be held on Tuesday, with music, but no speeches. For Wednesday a special wine-tasting party has been arranged. The Radium Chemical Company, Atomic Energy of Canada, Ltd., Varian Corporation and Applied Radiation Corporation are gracious hosts for several of these events. Unstructured social activities available every day include golf, tennis, swimming, ice-skating, handball, squash, skeet-shooting and fishing. Members and guests will find it difficult to make even one complete inspection of all the hotel's attractions in the few days available. There are 5 different restaurants to visit without even leaving the premises.

As always, registration is open to all who are interested. Advance registration by mail is suggested to avoid congestion and delays. There is no fee for members or for those who can be identified as residents in training. All who have participated in preparing the program are pleased with its development and we look forward to seeing you in Colorado Springs.

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THE AMERICAN RADIUM SOCIETY

FIFTY-FIFTH ANNUAL MEETING

BROADMOOR HOTEL, COLORADO SPRINGS
APRIL 22–26, 1973

PRELIMINARY PROGRAM

Sunday April 22, 1973

9:00 A.M.–12:00 P.M. Executive Committee Meeting
2:00–5:00 P.M. Registration
6:00 P.M. Welcoming Reception

Monday April 23, 1973

8:30 A.M. Opening ceremonies
8:40 A.M. President's Address. A. Raventos, M.D. University of California, Davis, California.

9:00 A.M.–1:00 P.M. FIRST SCIENTIFIC SESSION

Symposium: Diagnosis and Control of Lymphatic Dissemination of Pelvic Malignancies.
Moderator: George C. Lewis, Jr., M.D., Hahnemann Medical College, Philadelphia, Pennsylvania.
Speakers: Larry McGowan, M.D., Washington, D.C.
Gerald E. Hanks, M.D., Sacramento, California.

Intermission

Presiding: James F. Nolan, M.D., Los Angeles Tumor Institute, Los Angeles, California.

Correlation of histopathology with clinical results following radiation therapy for carcinoma of the cervix. Leonard L. Gunderson, M.D., Richard M. Hebertson, M.D., William Weems, M.D., and Henry P. Plenk, M.D., Latter-Day Saints Hospital, Salt Lake City, Utah.

A sequential study on the effect of the addition of hyperbaric oxygen on the five-year survival rates of carcinoma of the cervix treated with conventional fractionation irradiation. Richard J. Johnston, M.D., Lahey Clinic Foundation, Boston, Massachusetts, and R. J. Walton, M.B.B.S., Manitoba Cancer Treatment and Research Foundation, Winnipeg, Canada.

Radiotherapy for adenocarcinoma of the ovary. John Fazekas, M.D., and John G. Maier, M.D., George Washington University Medical Center, Washington, D.C.

Carcinoma of the bladder. Professor Brigit van der Werf-Messing, Scientific Director, Radiotherapy Institute, Rotterdam, Netherlands (Guest Speaker).

Simple mastectomy and radiation therapy for locally advanced breast cancers technically suitable for radical mastectomy. George R. Brown, M.D., Jean-Claude Horiot, M.D., and Gilbert Fletcher, M.D., M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

Resident Award winning paper.
(To be selected)

6:00 P.M. Reception for Members and Guests.
Hosts: Atomic Energy of Canada Limited.
7:00 P.M. The Broadmoor Western Dinner and Entertainment.

Tuesday April 24, 1973

7:45 A.M. First Executive Session for all Members. Breakfast.

9:00 A.M.–1:00 P.M. SECOND SCIENTIFIC SESSION

Symposium: Recent Developments in Fast Neutron Teletherapy.
Moderator: James T. Brennan, M.D., Matthew J. Wilson Professor of Research Radiology, University of Pennsylvania, Philadelphia, Pennsylvania.
Speakers: Charles Rogers, M.D., Medical College of Virginia, Richmond, Virginia.
Gilbert Fletcher, M.D., University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston, Texas.
Robert Parker, M.D., Seattle, Washington.

Intermission

Presiding: John V. Blady, M.D., Philadelphia, Pennsylvania.

Influence of fractionation on acute and late reactions in vocal cord carcinoma. R. Kenneth Loeffler, M.D., Massillon, Ohio.

Treatment and results of glottic carcinoma by megavoltage radiation therapy. C. C. Wang, M.D., Massachusetts General Hospital, Boston, Massachusetts.

Aggressive management of advanced head and neck tumors: technique, results and complications. S. Rafla, M.D., and J. Bochetto, M.D., Methodist Hospital, Brooklyn, New York.

Surgical management of cancer of the glottic region, recurrent after irradiation. A. J. Ballantyne, M.D., Gilbert H. Fletcher, M.D., and Jean Claude Horiot, M.D., University of Texas M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

THE JANEWAY LECTURE

Juan A. del Regato, M.D., Penrose Cancer Hospital, Colorado Springs, Colorado.

Introduction by Milford Schulz, M.D.

6:00 P.M. Reception for Members and Guests. Hosts: Radium Chemical Company.
7:00 P.M. Annual Banquet. Entertainment.

Wednesday April 25, 1973

7:45 A.M. Second Executive Session for all Members. Breakfast.

9:00 A.M.–1:00 P.M. THIRD SCIENTIFIC SESSION

Presiding: James T. Helsper, M.D., Pasadena Tumor Institute, Pasadena, California.

Investigative therapeutics in clinical oncology: RTOG protocol strategies. Philip Rubin, M.D., University of Rochester, Rochester, New York.

An evaluation of the effects of splenectomy in Hodgkin's disease in patients undergoing total nodal irradiation. R. L. Royster, Jr., M.D., E. R. King, M.D., J. E. Ebersole, M.D., and M. G. Bolin, M.D., Medical College of Virginia, Richmond, Virginia, and National Naval Center, Bethesda, Maryland.

The incidence of complications in laparotomy for Hodgkin's disease in children. Giulio D'Angio, M.D., and William B. Kiesewetter, M.D., Memorial Hospital, New York, New York.

The management of nodal recurrence following radical treatment in Hodgkin's disease and lymphoma. Philip Rubin, M.D., Richard Antemann, M.D., Henry Keys, M.D., and Eric Mayer, M.D., University of Rochester, Rochester, New York.

"Extended mantle field" in radiotherapy of patients with malignant lymphoma. Melvin L. Griem, M.D., John E. Ultmann, M.D., James E. Marks, M.D., and Edgar Moran, M.D., Department of Medicine (Hematology), Department of Radiology and the Argonne Cancer Research Hospital, University of Chicago, Chicago, Illinois.

Intermission

Radical radiation therapy and pelvic node dissection in cancer of the prostate. Basil Hilaris, M.D., Willet F. Whitmore, M.D., Mostafa Batata, M.D., and Harry Grabstald, M.D., Memorial Hospital, New York, New York.

The early lymphatic spread of manifest prostatic adenocarcinoma. Sulabha Masih, M.D., Mary Lou Ozohan, M.D., Samuel S. Kurohara, M.D., and Frederic W. George, III, M.D., Los Angeles County–University of Southern California, Los Angeles, California.

GUEST LECTURE

Cancer of the prostate. Professor Brigit van der Werf-Messing, Scientific Director, Radiotherapy Institute, Rotterdam, Netherlands.

GUEST LECTURE

Surgery of head and neck cancer in relation to radiotherapy. Ronald W. Raven, O.B.E., T.D., F.R.C.S., Consulting Surgeon, Royal Marsden Hospital and Cancer Institute, Consulting Surgeon, Westminster Hospital, Chairman of the Marie Curie Memorial Foundation for Cancer, Chairman of the British Association of Surgical Oncologists, London, England.

5:00 P.M. Special wine tasting and social hour.
6:00 P.M. Dinner by individual arrangement.

Thursday April 26, 1973

7:45 A.M. Third Executive Session for all Members. Breakfast.

9:00 A.M.–1:00 P.M. FOURTH SCIENTIFIC SESSION.

Symposium: Radium Protection.
Moderator: H. M. Parker, F. Inst. P., Battelle Pacific Northwest Laboratories, Richland, Washington.
Speakers: Relevant standards activities. H. M. Parker.
Radium in man. Robley D. Evans, Ph.D., Massachusetts Institute of Technology, Cambridge, Massachusetts.
Radium substitutes. Norman Simon, M.D., New York, New York.
Practical problems. Robert O. Gorson, Jefferson University Hospital, Philadelphia, Pennsylvania.
Clinical difficulties. A. Raventos, M.D., University of California, Davis, California.

Intermission

Presiding: Giulio D'Angio, M.D., Memorial Hospital, New York, New York.

Multifractionated, high dose-rate intracavitary radiation therapy: two years' experience with the brachytron. C. F. von Essen, M.D., David G. Seay, M.B., F.F.R., John Moeller, M.S., and Jerald W. Hilbert, Ph.D., University Hospital, San Diego, California.

Computerized radiation treatment planning with ultrasound. Donn J. Brascho, M.D., Department of Therapeutic Radiology, University of Alabama School of Medicine, Birmingham, Alabama.

The time-dose factors in radiation-induced osteitis. J. H. Kin, F.C.H. Chu, R. A. Pope, H. Q. Woodard, D. B. Bragg, and H. Shidnia, Memorial Hospital, New York, New York.

The treatment of malignant astrocytomas. Justin J. Stein, M.D., University of California Center for the Health Sciences, Los Angeles, California.

The present outlook for the patient with cancer of the colon and rectum. Bernard Roswit, M.D., and George A. Higgins, M.D., Veterans Administration Hospital, Bronx, New York.

A system for the clinical classification of lung cancer. Clifton F. Mountain, M.D., M. D. Anderson Hospital and Tumor Institute, Houston, Texas.

The second sac: a complicating factor in regimens based on intrathecal medications. Edward E. Rogoff, M.D., Michael D. F. Deck, M.B.B.S., and Giulio D'Angio, M.D., Memorial Hospital, New York, New York.

1:00 P.M. Adjournment of Fifty-fifth Annual Meeting.

INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION (ICRP)

THE International Commission on Radiological Protection (ICRP), after its meeting in November 1972, issued the following statement:

At its meeting in 1969 the Commission decided to re-examine the adequacy of its system of dose limits. For this purpose it initiated a close examination of the available information on estimates of risks from ionizing radiation, of the exposures actually received on the basis of the present dose limits, of the levels of safety achieved in existing safe industrial and other practices which do not involve exposure to radiation, and of the risks incurred in everyday life. As a result of this review the Commission does not see grounds for making any reduction in its dose limits for exposures of the whole body or of individual organs, either for workers or for members of the general public. In fact, it recognizes that the limits for red bone-marrow and gonads might appropriately be raised to a moderate extent to become consistent with the levels adopted for the whole body and for other tissues. It does not, however, regard it as necessary to modify the existing system of dose limits by recommending an immediate increase in these limits.

An important feature of the Commission's recommendations is the requirement "that all doses be kept as low as is readily achievable, economic and social considerations being taken into account." The application of this requirement has had a considerable influence in keeping exposures low, and it has been particularly effective in limiting the dose to individual members of the public and the dose to the total population. However, the Commission recognizes that it is not easy to interpret the requirement in a consistent manner and is therefore developing a report explaining in greater detail how it intends that the requirement should be applied and giving guidance on its practical implementation. This process includes a review of each operation with the aim of ensuring that the design and operating methods are such that the exposures are reduced to the point where the effort needed to achieve a further reduction is judged to involve economic and social costs that exceed the economic and social gains to be expected from the reduction. It is emphasized that exposures to radiation must be justifiable in terms of the associated benefits.

The Commission's Recommendations remain as set out in ICRP Publication 9,[1] as modified by subsequent amendments.[2,3] During the coming year the Commission will consider the need for a replacement of ICRP Publication 9 for issue by about 1976.

For further information please write to F. D. Sowby, M.D., Scientific Secretary, ICRP, Clifton Avenue, Sutton, Surrey, England.

[1] Recommendations of the International Commission on Radiological Protection. (Adopted September 17, 1965), ICRP Publication 9, Pergamon Press, Oxford (1966).
[2] *Health Phys.*, 1969, *17*, 389–390.
[3] *Health Phys.*, 1971, *21*, 615–616.

NEWS ITEMS

NEWER TECHNIQUES AND TECHNOLOGY IN RADIATION THERAPY AND CLINICAL ONCOLOGY

The Postgraduate Division of the University of Southern California School of Medicine is planning a program on "Newer Techniques and Technology in Radiation Therapy and Clinical Oncology," to be held at the Louis B. Mayer Medical Teaching Center, 2025 Zonal Avenue, Los Angeles, California, on February 16 and 17, 1973.

For further information please write to P. R. Manning, M.D., Associate Dean, Postgraduate Medical Education, 2025 Zonal Avenue, Los Angeles, California 90033.

ASPEN SEMINAR ON RADIOLOGY OF THE URINARY TRACT

(With a Session on Renal Osteopathies)

This Aspen Seminar is sponsored by The Department of Radiology, Louisiana State University School of Medicine in Shreveport and will be held, February 24–28, 1973, at the Aspen Institute for Humanistic Studies, Aspen, Colorado.

The Seminar is designed primarily for radiologists and urologists. The presentations will include discussions on radiologic evaluation and clinical management of neoplastic, inflammatory and traumatic conditions of the kidneys, ureters, bladder and urethra. A special session on "Renal Osteopathies" will deal with osseous manifestations encountered with disease afflicting the urinary tract. Discussions of various special radiologic techniques for study of the kidney, ureter, bladder and urethra including angiography, pharmacoangiography, magnification angiography, renal venography and isotopic examinations will be presented. Clinicians will discuss desirability and optimal and necessary degree of diagnostic pursuit for the management of various urologic conditions. The presentations will consist of formal talks, panel discussions attempting to analyze and summarize presented material and round table discussions offering the registrants an opportunity for free exchange of opinion with the panelists.

Sessions will be held in the early morning, late afternoon and evening.

An outstanding Guest Faculty is assembled for the Seminar under the direction of Dr. Erich K. Lang, Professor and Head, Department of Radiology, Louisiana State University School of Medicine in Shreveport.

The Guest Faculty will include: C. E. Carlton, Jr., M.D., Houston, Texas; Milton Elkin, M.D., New York, New York; John A. Evans, M.D., New York, New York; Richard M. Friedenberg, M.D., New York, New York; Harold Jacobson, M.D., New York, New York; Wyland F. Leadbetter, M.D., Boston, Massachusetts; Jorgen U. Schlegel, M.D., New Orleans, Louisiana; Russel Scott, M.D., Houston, Texas; Elias Theros, M.D., Washington, D.C.; Manuel Viamonte, Jr., M.D., Miami, Florida; Maria Viamonte, M.D., Miami Beach, Florida; and Keith R. Waterhouse, M.B., New York, New York; in addition to the staff of the Departments of Radiology and Urology of the LSU School of Medicine in Shreveport, Shreveport, Louisiana.

For further information please contact: E. K. Lang, M.D., Department of Radiology, LSU Medical Center, School of Medicine in Shreveport, P.O. Box 3932 Shreveport, Louisiana 71130.

SPRING ROENTGEN CONFERENCE

The New Orleans Radiology Society announces that its "Spring Roentgen Conference" will be held at Marriott Hotel, New Orleans, Louisiana, April 27 and 28, 1973.

The Guest Faculty includes James H. Christie, M.D., Iowa City, Iowa, on

Nuclear Medicine; Sidney W. Nelson, M.D., Columbus, Ohio, on Gastrointestinal Tract; Elias P. G. Theros, M.D., Bethesda, Maryland, on Chest; William Martel, M.D., Ann Arbor, Michigan, on Bone; and Charles E. Shopfner, M.D., Birmingham, Alabama, on Genitourinary Tract.

For further information please write: Abner M. Landry, M.D., New Orleans Radiology Society, P.O. Box 19024, New Orleans, Louisiana 70179.

SYMPOSIUM RADIOLOGICUM PANCREATIS

The date of the Symposium Radiologicum Pancreatis, which was announced in the September 1972 issue (Vol. 116, No. 1, p. 217) of this JOURNAL was changed because of technical reasons to May 26–29, 1973.

For registration and further information please contact, Prof. Dr. H. Anacker, Institut für Röntgendiagnostik der Technischen Universität München, Klinikum rechts der Isar, Ismaningerstrasse 22, 8 München 80, West Germany.

WORKING PARTY ON RADIONUCLIDES AND AFTERLOADING

Techniques in the Treatment of Cancer of the Uterus

The Working Party on Radionuclides and Afterloading Techniques in the Treatment of Cancer of the Uterus in developing areas, and The Ministry of Health of Brazil, with the co-sponsorship of The Bureau of Radiological Health of the US Department of Health, Education and Welfare, The British Institute of Radiology, The Faculty of Radiologists of Great Britain, The Mount Sinai School of Medicine, New York, The Middlesex Hospital Medical School, London, Circulo Latinamericano de Radioterapeutas, and The American Society of Therapeutic Radiologists announce a conference to be held during the Fourth Encontro of Radiotherapists and Physicists of Brazil June 4–June 6, 1973, at the National Cancer Institute of Brazil, Rio de Janeiro, Brazil.

The Working Party members are radiotherapists from more than 20 countries who previously convened in Geneva at WHO headquarters in February 1972 to discuss the intracavitary treatment of cancer of the uterus in developing areas. The Working Party will meet once again from May 30–June 1, 1973, preceding the Fourth Encontro of Radiotherapists and Physicists of Brazil, and the members will remain to lecture to the attendees of the Encontro.

The problems associated with the treatment of cancer of the uterus in many regions of the world will be presented and discussed. There will also be discussions on devices available for intracavitary irradiation of the pelvis, suitable radionuclides as substitutes for radium, simple and complex methods of afterloading and remote loading, and the status of computer dosimetry. Opportunity will be provided for informal discussions.

The Co-Chairmen are: Norman Simon, M.D., Mount Sinai School of Medicine, New York, New York 10029, U.S.A., and Margaret Snelling, F.R.C.P., Meyerstein Institute of Radiotherapy, The Middlesex Hospital, London W1N 8AA, England.

The Coordinator is Moacyr Santos-Silva, M.D., Director, Ministerio Da Saude, Divisão Nacional De Cancer, Rio de Janeiro, Brazil.

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (WHO)

Lyon, France

Application for training fellowships in 1973–1974 are invited from junior scientists wishing to be trained in any aspect of laboratory and clinical cancer research. The Agency is especially interested in receiving applications for training in epidemiology, biostatistics and all aspects of environmental biology.

Applicants should be engaged in research in medical or allied sciences and intend to pursue a career in cancer research.

Fellowships are awarded for one year and are tenable in a suitable institution abroad. Fellows will, in general, be selected

from applicants with less than five years postdoctoral experience in medicine or the natural sciences. They must have an adequate knowledge, both written and spoken, of the language of the country in which their fellowship is tenable.

Applications cannot normally be accepted from people already holding fellowships enabling them to study abroad.

Stipends will vary according to the cost of living in the country of study. The cost of travel for the applicant and, in certain circumstances, that of his wife and children, will be met.

Applications must reach the Agency not later than 28 February 1973.

Fellowship application forms and more detailed information are available from: The Chief of the Research Training and Liaison Unit, International Agency for Research on Cancer, 150, cours Albert-Thomas, 69008 Lyon, France.

BOOK REVIEW

Sectional Anatomy and Tomography of the Head. By Guy D. Potter, M.D., Associate Professor of Radiology, College of Physicians and Surgeons, Columbia University and the Columbia-Presbyterian Medical Center, New York, New York. Cloth. Pp. 334, with many illustrations. Price, $30.00. Grune & Stratton, Inc., New York, New York, 1971.

The author has designed an exceptional atlas of the normal tomographic anatomy of the head. Line drawings identify individual structures of the various roentgenograms of 145 sections, with each section being 1 mm. thick. Coronal, lateral, axial and oblique projections are shown.

An index of important intracranial structures and the views that they can be found in, is presented.

The reader obtains a three-dimensional concept of the anatomy and learns important intracranial relationships.

This book is highly recommended for all radiologists and other specialists working with head and neck problems.

Harvey I. Wilner, M.D.

BOOKS RECEIVED

Clinical Dynamic Function Studies with Radionuclides. Edited by Millard N. Croll, M.D., Associate Professor of Radiology, Department of Radiation Therapy and Nuclear Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pa.; Luther W. Brady, M.D., Professor of Radiology and Chairman, Department of Radiation Therapy and Nuclear Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pa.; H. Randolph Tatem, III, M.D., Attending in Radiology, Doylestown Hospital, Doylestown, Pa.; and Takashi Honda, M.D., Research Assistant Professor of Radiology, Department of Radiation Therapy and Nuclear Medicine, Hahnemann Medical College and Hospital, Philadelphia, Pa. Cloth. Pp. 307, with some illustrations. Price, $18.50. Appleton-Century-Crofts, 440 Park Avenue South, New York, N. Y. 10016, 1972.

Gastrointestinal Angiography. By Stewart R. Reuter, M.D., Professor of Radiology, University of Michigan School of Medicine, Ann Arbor, Mich.; Director, Department of Radiology, Wayne County General Hospital, Eloise, Mich.; Formerly, Associate Professor of Radiology, University of California, San Diego, Calif.; and Helen C. Redman, M.D., Assistant Chief, Department of Radiology, Mt. Zion Hospital, San Francisco, Calif.; Clinical Associate Professor of Radiology, University of California School of Medicine, San Francisco, Calif.; Clinical Associate Professor of Radiology, Stanford University School of Medicine, Palo Alto, Calif.; Formerly Associate Professor of Radiology, University of Michigan School of Medicine, Ann Arbor, Mich., at Wayne County General Hospital, Eloise, Mich. Cloth. Pp. 292, with 268 figures. Price $17.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1972.

Exercises in Diagnostic Radiology. Volume 4: The Total Patient. By Lucy Frank Squire, M.D., Lecturer on Radiology, Harvard Medical School; Visiting Radiologist, Massachusetts General Hospital, Boston; Professor in Radiology, Downstate Medical Center, Brooklyn, N. Y.; Jack R. Dreyfuss, M.D., Associate Clinical Professor of Radiology, Harvard Medical School; Radiologist, Massachusetts General Hospital, Boston; Charles S. Langston, M.D., Instructor in Radiology, Harvard Medical School; Assistant in Radiology, Massachusetts General Hospital, Boston; and Robert A. Novelline, M.D., Clinical Fellow in Radiology, Harvard Medical School; Resident in Radiology, Massachusetts General Hospital, Boston. Paper. Pp. 139, with 173 illustrations. Price, $5.95. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1972.

Roentgenography and Roentgenology of the Temporal Bone, Middle Ear and Mastoid Process. Second edition. By Lewis E. Etter, B.S., M.D., F.A.C.R., Professor of Radiology, Western Psychiatric Institute and Clinic, the Falk Clinic, Presbyterian University Hospital School of Medicine, University of Pittsburgh; Consultant, C. Howard Marcy State Hospital, Pittsburgh, Pa. Cloth. Pp. 211, with many figures. Price, $17.00. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62717, 1972.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 25–28, 1973.

AMERICAN RADIUM SOCIETY
Secretary, Dr. Felix N. Rutledge, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025. Annual Meeting: Broadmoor Hotel, Colorado Springs, Colorado, April 22–26, 1973.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. Hillier L. Baker, Jr., Mayo Clinic, Rochester, Minn. 55901. Annual Meeting: Palmer House, Chicago, Ill., November 25–30, 1973.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago, Ill. 60606. Annual meeting: San Francisco, Calif., April 2–7, 1973.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Antolin Raventos, Davis, Calif. Annual Meeting: New York, N. Y., June 24–28, 1973.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler East, Rochester, Minn. 55901.

Oral examinations will be held in the following cities during the next year: Chicago, Ill., June 4–8, 1973, Marriott Motor Hotel; and Dallas, Tex., Dec. 3–7, 1973, Statler Hilton Hotel.

Written examinations are scheduled in 13 large centers.

Applications must be received in the Board Office before Sept. 30 of the year preceding the one in which the candidate wishes to be examined.

Deadline for filing applications for any examination in 1973 was September 30, 1972.

AMERICAN BOARD OF NUCLEAR MEDICINE, INC. A Conjoint Board of the American Boards of Internal Medicine, Pathology and Radiology and sponsored by the Society of Nuclear Medicine.

Chairman, Dr. Merrill A. Bender, Suite 2402, 211 E. 43rd St., New York, N. Y. 10017.

Examination for certification in the Specialty of Nuclear Medicine will be given April 7, 1973. The deadline for filing application forms was January 1, 1973.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, D. John Wright, Ph.D., Department of Radiology, Temple Univ. Health Sciences Center, Philadelphia, Pa. 19140. Annual Meeting in San Diego, Calif., July 29–Aug. 3, 1973.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. Herman D. Suit, Radiation Medicine, Massachusetts General Hospital, Boston, Mass. 02114. Annual Meeting.

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE
Secretary, John M. Reid, Ph.D., 556 18th Ave., Seattle, Wash. 98122. Annual Meeting.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary, Dr. David O. Davis, Department of Radiology, 901 Twenty-third St., N. W., Washington, D. C. 20037. Annual Meeting, Boston, Mass., April 26–28, 1973.

THIRTEENTH INTERNATIONAL CONGRESS OF RADIOLOGY
President-Elect, Dr. Juan Gómez López. *Secretary General*, Dr. José Bonmatí, Lagasca, 27 Madrid 1, España. Meeting: Madrid, Spain, Oct. 15–20, 1973.

INTERNATIONAL SOCIETY OF RADIOLOGY
Hon. Secretary-Treasurer, Prof. Eric Samuel, Radiologist-in-Charge, The Royal Infirmary, Edinburgh EH3 9Y-W, Scotland.

ELEVENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colorado 80907. Meeting: Bogotá, Colombia in 1975.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Miguel Dao y Dao, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A.
Secretary General, Dr. Rubén Merenfeld, Instituto Diagnóstico, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A. Meeting: Bogotá, Colombia in 1975.

THIRD CONGRESS OF THE EUROPEAN ASSOCIATION OF RADIOLOGY
Meeting in June, 1975 in Edinburgh, Scotland.

SECOND ASIAN AND OCEANIAN CONGRESS OF RADIOLOGY
Honorary Secretary, Dr. J. J. Martin, Box 805 F., G.P.O., Melbourne, 3001, Australia.
Meeting in 1975.

ALABAMA CHAPTER OF ACR
Secretary-Treasurer, Dr. Lowry R. Young, Jr., 905 Madison St., Huntsville, Ala. 35801. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

AMERICAN THERMOGRAPHIC SOCIETY
Secretary-Treasurer, Dr. Marc. S. Lapayowker, Department of Radiology, Temple Univ. Hosp., 3401 N. St., Philadelphia, Pa. 19140. Meets at New York-Hilton Hotel, June 23 and 24, 1973.

ARIZONA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Wesley S. Fee, 2421 E. 6th St., Tucson, Ariz. 85719. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARK-LA-TEX RADIOLOGICAL SOCIETY
Secretary, Dr. Erich K. Lang, Confederate Memorial Medical Center, LSU School of Medicine, Shreveport, La. 71101.

ARKANSAS CHAPTER OF ACR
Secretary-Treasurer, Dr. David H. Newbern, 4301 W. Markham, Little Rock, Ark. 72205. Meets twice annually, the Spring Meeting being in conjunction with and at the place of the State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Melvyn H. Schreiber, 2909 Dominique Dr., Galveston, Tex. Annual Meeting, Vancouver, B. C., Canada, May 9–12, 1973.

ATLANTA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Ernst Ruder, Dept. of Radiol., Crawford Long Memorial Hosp., Atlanta, Ga. 30308. Meets on four Thursday evenings during the academic year at a time announced in early September of each year, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Secretary, Lucien F. Burke, Maj. MC, Radiol. Service, US Army Gen. Hosp., Frankfurt, APO, New York 09757.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Eugene Slusher, Lexington

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Clinic, 1221 S. Broadway, Lexington, Ky. 40504. The Society meets once each month during the school year.

Bronx Radiological Society, New York State, Chapter ACR
Secretary-Treasurer, Dr. Leon J. Corbin, 1369 Rosedale Ave., Bronx, N. Y. 10472. Meets 4 times a year.

Brooklyn Radiological Society
Secretary-Treasurer, Dr. Sarah Lieberson, 1298 St. Marks Ave., Brooklyn, N. Y. 11213. Meets first Thursday of each month, October through June.

Buffalo Radiological Society
Secretary, Dr. Ru-Kan Lin, 191 North St., Buffalo, N. Y. 14201. Meets second Monday evening each month, October to May inclusive, at University Club.

California Radiation Therapy Association
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets semiannually in San Francisco and Los Angeles.

California Radiological Society, California Chapter of ACR
Secretary-Treasurer, Dr. John L. Gwinn, 4650 Sunset Blvd., Los Angeles, Calif. 90027.

Catawba Valley Radiological Society
Secretary, Dr. Emmett R. White, P.O. Box 10, Rutherford College, N. C. 28671. Meets every Thursday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:30 P.M.

Central New York Radiological Society
Secretary-Treasurer, Dr. John Sanborn, Radiology Department, Crouse-Irving Memorial Hosp., Irving Ave., Syracuse, N. Y. 13210. Meets first Monday each month October through May.

Central Ohio Radiological Society
Secretary-Treasurer, Dr. Terry Meyer, 175 S. Merkle Rd., Columbus, Ohio 43209. Meets second Thursday in October, November, January, and March 15, and May 19 at Fort Hayes Hotel, Columbus, Ohio.

Chicago Radiological Society, Division of the Illinois Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Raymond L. Del Fava, 355 Ridge Ave., Evanston, Ill. 60202. Meets third Thursday of each month, October to April, except December, at the Bismarck Hotel, Chicago, Ill.

Cleveland Radiological Society
Secretary-Treasurer, Dr. Daniel E. Wertman, 11311 Shaker Blvd., Cleveland, Ohio 44104. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

Colorado Radiological Society, Chapter of ACR
Secretary, Dr. Jerome D. Sutherland, 3705 E. Colfax Ave., Denver, Colo. 80206. Meets third Friday of each month at Denver Athletic Club from September through May.

Connecticut Valley Radiologic Society
Secretary, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meets in April and October.

Dallas-Fort Worth Radiological Society
Secretary-Treasurer, Dr. Norman L. Presley, 222 Medical Tower, 1550 W. Rosedale, Fort Worth, Tex. 76104. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Tex.

Delaware Chapter of ACR
Secretary, Dr. Seymour R. Kaplan, Kent Gen. Hosp., Dover, Del. 19901.

East Bay Radiological Society
Secretary-Treasurer, Dr. Peter E. Kane, Children's Hosp. Med. Ctr., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

East Tennessee Radiological Society
Secretary-Treasurer, Dr. George H. Wood, 205 Medical Arts Bldg., Knoxville, Tenn. 37902. Meets in January and September.

Florida Radiological Society, Chapter of ACR
Secretary, Dr. Ralph C. Aye, Tampa General Hospital, Tampa, Fla. 33606. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. J. C. Hewitt, 1 Davis Blvd., Tampa, Fla. 33606. Meets in January, March, May, July, September and November.

Georgia Radiological Society, Chapter of ACR
Secretary, Dr. Richard S. Colvin, Emory University Clinic, Atlanta, Ga. 30322. Meets in spring and fall at Annual State Society Meeting.

Greater Cincinnati Radiological Society
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

Greater Louisville Radiological Society
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

Greater Miami Radiological Society
Secretary-Treasurer, Dr. Stanley I. Worton, 1400 N.W. 10th Avenue, Miami, Florida 33136. Meets monthly, third Wednesday at 8:00 P.M. at various member hospitals, Miami, Fla.

Greater St. Louis Society of Radiologists
Secretary-Treasurer, John J. Lang, 507 Fairways Circle, St. Louis, Mo. 63141.

Hawaii Radiological Society, Chapter of ACR
Secretary-Treasurer, Raymond W. Brust, Jr., St. Francis Hosp., 2260 Liliha St., Honolulu, Hawaii 96817. Meets third Monday of each month at 7:30 P.M.

Health Physics Society
Secretary, John H. Pingel, Argonne National Laboratory, 9700 S. Cass Ave., Argonne, Ill. 60439. Annual Meeting: Deauville Hotel, Miami Beach, Fla., June 17–21, 1973.

Houston Radiological Society
Secretary, Dr. Neill B. Longley, 6436 Fannin, Suite 601, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

Idaho State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Hugh P. Smith, Jr., 130 E. Bannock, Boise, Id. 83702. Meets in the spring and fall.

Illinois Radiological Society, Inc., Chapter of ACR
Secretary, Dr. B. Jay Hill, Mercy Hospital, Stevenson at King Drive, Chicago, Ill. 60616. Meets in the spring and fall.

Indiana Roentgen Society, Inc., Chapter of ACR
Secretary, Dr. L. Ray Stewart, 852 S. Alvord Blvd., Evansville, Ind. 47714.

Iowa Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John Huston Jr., 1948 First Ave. N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ralph H. Baehr, 310 Medical Arts Bldg., Topeka, Kan. 66604. Meets in spring with State Medical Society and in winter on call.

Kentucky Chapter of ACR
Secretary-Treasurer, Dr. Joseph G. Whelan, Jr., 1313 St. Antony Place, Louisville, Ky. 40204. Meets in April and September.

Kings County Radiological Society
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N.Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Knoxville Radiological Society
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

Long Island Radiological Society
Secretary, Dr. Jerome Zwanger, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

LOS ANGELES RADIOLOGICAL SOCIETY
Secretary, Dr. Gabriel H. Wilson, UCLA Center for Medical Sciences, Los Angeles, Calif. 90024. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif. Midwinter Radiological Conference, Century Plaza Hotel, Los Angeles, Calif. 90067, Feb. 2–4, 1973.

LOUISIANA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Robert T. Cook, Southern Baptist Hosp., 2700 Napoleon Ave., New Orleans, La. 70115.

LOUISIANA-TEXAS GULF COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Tex. 77701.

MAINE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Richard W. Taylor, Radiology Department, St. Mary's General Hospital, Lewiston, Maine 04240. Meets in June, September, December and April.

MARYLAND RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. George Burke, 4000 North Charles St., Baltimore, Md. 21218.

MASSACHUSETTS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Norman L. Sadowsky, The Faulkner Hosp., 1153 Centre St., Jamaica Plain, Mass. 02130.

MEMPHIS ROENTGEN SOCIETY
Secretary-Treasurer, Dr. Jerry C. Phillips, The University of Tennessee College of Medicine, Department of Radiology, Walter C. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday Oct. through May at the University Club.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Ind. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

MICHIGAN RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. George A. Kling, Harper Hospital, 3825 Brush St., Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary-Treasurer, Dr. Thomas C. Lipscomb, 1004 North Tenth St., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

MINNESOTA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Harlan W. Hawkinson, 6 Buffalo Rd., St. Paul, Minn. 55110. Meets twice annually, fall and winter.

MISSISSIPPI STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Nancy W. Burrow, 1327 Peachtree St., Jackson, Miss. 39202. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

MISSOURI RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ronald G. Evens, Mallinckrodt Institute of Radiology, 510 S. Kingshighway, St. Louis, Mo. 63110.

MONTANA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Dexter W. Johnson, Columbus Hosp., Great Falls, Mont. 59401.

NEBRASKA CHAPTER OF ACR
Secretary-Treasurer, Dr. John T. McGreer, III, 924 Sharp Bldg., Lincoln, Nebr. 68508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEVADA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. William G. Arbonies, 887 Marsh, Reno, Nev. 89520.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stefan C. Schatzki, 1180 Beacon St. Brookline Mass. 02146. Meets the third Friday of each month, October through April, excluding December, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Edward P. Kane, Claremont Gen. Hosp., Claremont, N. H. 03743. Meets four to six times yearly.

NEW MEXICO SOCIETY OF RADIOLOGISTS, CHAPTER OF ACR
Secretary, Dr. Carole R. Simmons, Dept. of Radiol., Presbyterian Hospital Center, Albuquerque, N. M. 87106. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

NEW ORLEANS RADIOLOGICAL SOCIETY, INC.
Secretary-Treasurer, Dr. Jimmy L. Mains, P.O. Box 446, Gretna, La. 70053. Meets bimonthly at local restaurants selected by the President.

NEW YORK ROENTGEN SOCIETY
Secretary-Treasurer, Dr. Howard R. Gould, 153 West 11th Street, New York, N. Y. 10011. Meets monthly on the 3rd Monday at the New York Academy of Medicine at 4:30 P.M. Annual Spring Conference, Waldorf-Astoria Hotel, New York, N. Y., Apr. 26–28, 1973. Further information may be obtained from Dr. Albert A. Dunn, Roosevelt Hosp., New York, N. Y. 10019.

NEW YORK STATE CHAPTER OF ACR
Secretary-Treasurer, Dr. John J. Magovern, 74 N. Village Ave., Rockville Centre, N. Y. 11570.

NORTH CAROLINA CHAPTER OF ACR
Secretary-Treasurer, Dr. James F. Martin, 300 S. Hawthorne Road, Winston-Salem, N. C. 27103.

NORTH DAKOTA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Marshall Landa, 1702 13th St., So., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

NORTH FLORIDA RADIOLOGICAL SOCIETY
Secretary, Dr. David F. Bew, University Hospital of Jacksonville, 655 W. Eighth Street, P.O. Box 2751, Jacksonville, Florida 32203. Meets quarterly in March, June, September and December.

NORTHEASTERN OKLAHOMA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Theodore J. Brickner, Jr., 5919 S. Gary Place, Tulsa, Okla. 74110.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. Robert C. Friedman, 325 Presidential Way, Guilderland, N. Y. 12085. Meets in Albany area on third Wednesday of October, November, March, April, and May.

NORTHERN CALIFORNIA RADIATION THERAPY ASSOCIATION
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets quarterly.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. Richard McProuty, 6620 Coyle Ave., Carmichael, Calif. 95608. Meets fourth Monday of Nov., Jan., and March at the Mansion Inn, Sacramento, Calif.

NORTHWESTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. Barbara E. Chick, Glens Falls Hospital, Glens Falls, N. Y. 12801.

NORTHWESTERN OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

OHIO STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Thomas F. Ulrich, Barberton Citizens Hospital, Barberton, Ohio 44203.

OKLAHOMA STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. George H. Ladd, 4616 Denison, Muskogee, Okla. 74401. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Norman Arnett, 400 North Pomona, Fullerton, Calif. 92632. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

Oregon State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ronald W. Philips, 2305 Washington, Milwaukie, Ore. 97222. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Oregon 97005. Annual meeting: Benson Hotel, Portland, Ore., May 11–13, 1973.

Pennsylvania Radiological Society, Chapter of ACR
Secretary, Dr. Theodore A. Tristan, Harrisburg Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. Howard M. Pollack, Department of Radiology, Episcopal Hospital, Philadelphia, Pa. 19125. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Stephen C. Bruno, Shadyside Hospital, 5230 Centre Ave., Pittsburgh, Pa. 15232. Meets second Wednesday of month, October through June, at Park Schenley Restaurant.

Radiation Research Society
Executive Secretary, Richard J. Burk, Jr., 4211 39th St., N.W., Washington, D. C. 20016. Annual Meeting: St. Louis, Mo., April 29–May 3, 1973. International Congress of Radiation Research, Seattle, Wash., July 14–20, 1974.

Radiological Society of Connecticut, Inc., Chapter of ACR
Secretary-Treasurer, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Alvin Nathan, c/o Academy of Medicine, 320 Broadway, Cincinnati, Ohio 45202. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
President-Secretary, Dr. Arch W. Templeton, Univ. of Kansas Med. Ctr., Kansas City, Kansas 66103. Meets 5 times a year on given dates.

Radiological Society of Louisiana, Chapter of ACR
Secretary-Treasurer, Dr. Robert T. Cook, 1820 Octavia St., New Orleans, La. 70115. Meets semiannually during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey, Chapter of ACR
Secretary, Dr. Sidney Ketyer, St. Elizabeth Hosp., 225 Williamson St., Elizabeth, N. J. 07207. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island, Chapter of ACR
Secretary-Treasurer, Dr. Daniel J. Hanson, 116 Nayatt Rd., West Barrington, R. I. 02806.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Marshall Rowen, Dept. Radiol., St. Joseph Hosp., 1100 Stewart Dr., Orange, Calif. 92668. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. Donald P. King, 218 Gun Club Rd., Richmond, Va. 23221. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary-Treasurer, Dr. Kenneth E. Robinson, 1441 East Avenue, Rochester, New York 14610. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Lorenz R. Wurtzebach, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 2–4, 1973.

San Antonio-Civilian Military Radiological Society
Secretary, Dr. Robert M. Maurer, Santa Rosa Medical Center, San Antonio, Tex. 78207. Meets third Wednesday of each month at Fort Sam Houston Officers' Club at 6:30 P.M.

San Diego Radiological Society
President, James R. Collins, 340 Fourth Ave. Suite 15, Chula Vista, Calif. 92010. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary-Treasurer, Dr. James G. Moore, Mary's Help Hospital, 1900 Sullivan Ave., Daly City, Calif. 94015.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section on Radiology, Southern Medical Association
Secretary, Dr. Mario A. Calonje, 1514 Jefferson Highway, New Orleans, La. 70121. Annual Meeting.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027. Annual meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 23–24, 1973.

Society of Gastrointestinal Radiologists
Secretary-Treasurer, Dr. Wm. B. Seaman, The Presbyterian Hospital, Columbia-Presbyterian Medical Center, 622 W. 168th St., New York, N. Y. 10032.

Society of Nuclear Medicine
Secretary, Dr. E. James Potchen, Edward Mallinckrodt Institute of Radiology, 660 S. Euclid Ave., St. Louis, Mo. 63110. *Administrative Officer*, Mrs. Margaret Glos, 211 E. 43rd St., New York, N. Y. 10017. Annual meeting: Americana Hotel, Miami Beach, Fla., June 12–15, 1973.

South Bay Radiological Society
Secretary, Dr. A. D. Benjamin, 596 Carroll St., Sunnyvale, Calif. 94086. Meets the 2nd Monday of each month at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

South Carolina Radiological Society, Chapter of ACR
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Coast Radiological Society
Secretary-Treasurer, Dr. James T. McClintock, P.O. Box 837, Santa Barbara, Calif. 93102. Meets fourth Monday of the month, Oct. through May.

SOUTH DAKOTA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. M. F. Petereit, 2416 S. Phillips, Sioux Falls, S. D. 57105. Meets in spring with State Medical Society and in fall.

SOUTHERN CALIFORNIA RADIATION THERAPY SOCIETY
Secretary-Treasurer, Dr. John Byfield, 1000 West Carson St., Torrance, Calif. 90502. Meets quarterly.

SOUTHERN RADIOLOGICAL CONFERENCE
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 7544, Mobile, Ala. 36607. Seventeenth Annual Meeting: Grand Hotel, Point Clear, Ala., Jan. 26–28, 1973.

SOUTHWESTERN RADIOLOGICAL SOCIETY
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

TENNESSEE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Carl T. Stubblefield, Bedford County Hospital, Columbia, Tenn. 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

TEXAS STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Herman C. Sehested, 815 Medical Tower, Room 100, 1550 W. Rosedale St., Fort Worth, Tex. 76104. Annual meeting.

THE FLEISCHNER SOCIETY
President, Dr. Robert G. Fraser, 1555 Summerhill Ave., Montreal 109, P.Q., Canada. Annual meeting.

TRI-STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

UPPER PENINSULA RADIOLOGICAL SOCIETY
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

UTAH STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. John F. Stucki, Department of Radiology, McKay-Dee Hosp., 3939 Harrison Blvd., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

VERMONT RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. J. Lorimer Holm, R.R. #3, Barre, Vt. 05641.

VIRGINIA CHAPTER OF ACR
Secretary-Treasurer, Dr. James S. Redmond, Suite 7, Medical Center, Lynchburg, Va. 24501. Next Meeting: Nov. 6, 1972 at the Conference Ctr., Williamsburg, Va.

WASHINGTON, D. C., CHAPTER OF ACR
Secretary-Treasurer, Dr. Albert M. Zelna, 9110 Seven Locks Rd., Bethesda, Md. 20014.

WASHINGTON STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. John N. Roehr, 1011 Medical Dental Bldg., Seattle, Wash. 98101.

WEST VIRGINIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Andrew W. Goodwin, II, 200 Med. Arts Bldg., Charleston, W. Va. 25301. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

WESTCHESTER COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Max C. King, 314 Woodland Hills Rd., White Plains, N. Y. 10603. Meets on second Tuesday of October, December, February and May.

WISCONSIN RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Marvin L. Hinke, 630 S. Central Ave., Marshfield, Wisc. 54449. Meets twice a year, May and September.

WISCONSIN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. Robert W. Edland, Gundersen Clinic, LaCrosse, Wisc. 54601. Meets quarterly.

WYOMING RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Ross J. Collie, Box 96, Lander, Wyo. 82520. Meets in fall with State Medical Society and in spring on call of President.

MEXICO, PUERTO RICO AND CENTRAL AMERICA

ASOCIACIÓN COSTARRICENSE DE RADIOLOGÍA
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

ASOCIACIÓN DE RADIÓLOGOS DE CENTRO AMERICA Y PANAMÁ. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá
Secretary-General, Dr. Francisco Mirambell, Apartado 3352, San José, Costa Rica, Central America.
Meets annually in a rotating manner in the six countries.

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

SOCIEDAD DE RADIOLOGÍA DE EL SALVADOR
Secretary, Dr. Carlos Mejia, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

SOCIEDAD DE RADIOLOGÍA DE GUATEMALA
Secretary, Dr. Carlos E. Escobar, 9². Calle A 0-05, Zona 1, Guatemala.

SOCIEDAD MEXICANA DE RADIOLOGÍA, A.C.
Coahuila No. 35, México 7, D.F., México.
Secretary-General, Dr. Jorge Cano Coquí. Meets first Monday of each month.

SOCIEDAD RADIOLÓGICA PANAMEÑA
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

SOCIEDAD RADIOLÓGICA DE PUERTO RICO
Secretary, Dr. Heriberto Pagán Sáez, Box 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

BRITISH COMMONWEALTH OF NATIONS

ASSOCIATION OF RADIOLOGISTS OF THE PROVINCE OF QUEBEC
Moyne, 121 Boul. Taschereau, Greenfield Park, P.Q., Canada. Meets four times a year.

BRITISH INSTITUTE OF RADIOLOGY
Honorary Secretary, Dr. T. Kerr, 32 Welbeck St., London, W1M/7PG, England. Meets monthly from October until May.

CANADIAN ASSOCIATION OF PHYSICISTS, DIVISION OF MEDICAL AND BIOLOGICAL PHYSICS
Honorary Secretary-Treasurer, Dr. R. G. Baker, Ontario Cancer Foundation, Ottawa Civic Clinic, 1053 Carling Ave., Ottawa 3, Ont., Canada.

CANADIAN ASSOCIATION OF RADIOLOGISTS
Honorary Secretary, Dr. Champlain Charest, 1555 Summerhill Ave., Montreal 109, Que., Canada. Annual meeting: Montreal, Que., Canada, March 11–17, 1973.

EDMONTON AND DISTRICT RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Koller, Suite 360, Professional Bldg., 10830 Jasper Ave., Edmonton 15, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

FACULTY OF RADIOLOGISTS
Honorary Secretary, Robert Morrison, 47 Lincoln's Inn Fields, London, W.C.2, England. The scientific meetings held in January, February and March 1973 will be combined sessions with the British Institute of Radiology and the Section of Radiology of The Royal Society of Medicine.

FACULTY OF RADIOLOGISTS, ROYAL COLLEGE OF SURGEONS IN IRELAND
Hon. Secretary, Dr. D. F. Canwell, 123 St. Stephens Green, Dublin 2, Ireland.

MONTREAL RADIOLOGICAL STUDY CLUB
Secretary, Dr. W. Paul Butt, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 8:15 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1 M&AE, 1 England.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Hubert Sasseville, Verdun Hospital, Montréal, P.Q., Canada. Meets every third Tuesday from October to April.

The Hospital Physicists' Association
Honorary Secretary, J. B. Massey, B.Sc., Christie Hosp. and Holt Radium Institute, Physics Department, Withington, Manchester M20 9BX, England.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

Royal College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, 147 Macquarie St., Sydney, N.S.W. 2000, Australia.

South America

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Federación Argentina de Sociedades de Radiología
Branches of the Federation are: Sociedad de Radiólogos de la Provincia de Córdoba; Sociedad Argentina de Radiología; Asociación Argentina de Radiología; Sociedad de Radiología, Radioterapéutica y Medicina Nuclear de Rosario; Sociedad de Radiología y Medicina Nuclear del Centro y Sudeste de la Provincia de Buenos Aires (Mar del Plata); Sociedad Salteña de Radiología y Medicina Nuclear; Sociedad de Radiología de Tucumán; Sociedad de Radiologia del Nordeste Argentino; Sociedad de Radiología de La Plata; and Sociedad de Radiología de San Juan.
Secretary-General-Treasurer, Dr. Roberto Habichayn, Av. Colón 637, Córdoba, Argentina.

Sociedad Argentina de Radiología
Secretary-General, Dr. Armando B. de Onaindia, Santa Fé 1171, Buenos Aires, Argentina. Meets first Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Caixa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Claudio Cortés, Casilla, 13426 Santiago, Chile. Meets first Friday of each month at Av. Santa María 1810 at 7:00 P.M.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Rodrigo Caro Molina, Cali, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología
Secretary, Dr. Carlos Palau Jimenez, Casilla 5469, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Hugo Volpe Rios, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dr. Miguel Chiappori Cambana, Av. General Santa Cruz No. 315, Miraflores, Lima, Perú, Casilla Correo, 2306, Lima, Perú. Meets monthly except during January, February, and March.

Sociedad de Radiología del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología del Nordeste Argentino
Secretary-General, Dr. Francisco J. Velar, Catamarca 561, Corrientes, Argentina.

Sociedad de Radiología de La Plata
Secretary, Dr. Hiram D. Haurigot, Calle 50 No. 374, La Plata, Argentina.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Manuel Gonzáles Maseda, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad de Radiología, Radioterapéutica y Medicina Nuclear, de Rosario
Secretary-General, Dr. Federico Frágola, Santa Fe 1798, Rosario, Argentina.

Sociedad Salteña de Radiología y Medicina Nuclear
Secretary, Dr. Julio Luis Baldi, Av. Sarmiento 536, Salta, Argentina.

Sociedad Venezolana de Radiología y Medicina Nuclear
Secretary-General, Dr. Salvador Itriago Borgas, Apartado Postal 9213, Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
Secretary, Dr. Ernst Kotcher, Wiener Allgemeine Poliklinik Mariannengasse 10, A-1090 Wien, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. The 1973 Annual Meeting is a joint meeting with the Deutsche Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belgium. Meets in February, March, May, June, September, October, November and December.

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Société Française de Radiologie Médicale, Médecine Nucléaire et Electrologie, and its branches: Société du Sud-Ouest, du Littoral méditerranéen, du Centre et Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et du Massif Central. Parent Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
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ABSTRACTS OF RADIOLOGIC LITERATURE

E. FREDERICK LANG, M.D., Editor

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ROENTGEN DIAGNOSIS

HEAD

ARCHER, CAROL R., ROBERSON, GLENN H., and TAVERAS, J. M. Posterior medullary hemangioblastoma. *Radiology*, May, 1972, *103*, 323–328. (From: Department of Radiology, Edward Mallinckrodt Institute of Radiology, Washington School of Medicine, St. Louis, Mo.)

The angiographic features of 3 cases of hemangioblastoma arising from the posterior aspect of the medulla oblongata are compared to a case of hemangioblastoma of the cerebellar tonsil.

The characteristic angiographic features of hemangioblastoma are a small dense tumor stain with early filling of draining veins and associated mass effect larger than the tumor stain. The medullary lesions produced separation of the posterior medullary segments and the choroidal loops of the posterior inferior cerebellar arteries (PICA). The tonsillar lesion stretched the supratonsillar segments and displaced the ipsilateral PICA branches to the opposite side across the midline

The area postrema of the dorsal medulla at the caudal end of the fourth ventricle is a frequent site of origin of hemangioblastoma in the posterior fossa.

Patients with infratentorial hemangioblastomas usually present in their third or fourth decade with symptoms due to increased intracranial pressure. Ipsilateral cerebellar signs are the most common physical finding. The familial occurrence of hemangioblastoma in 20 per cent of the cases suggests that it is but one manifestation of a systemic disorder due to maldevelopment. Multiplicity of lesions within the posterior fossa in 10 per cent of the cases, associated with angiomatosis retinae, adrenal, renal and pancreatic cysts, and hypernephroma, is also suggestive of maldevelopment.

The characteristic angiographic features associated with retinal angiomata are virtually pathognomonic for this tumor.—*J. L. Montgomery, M.D.*

NECK AND CHEST

SCOTT, ROY, DRYBURGH, FRANCES, WILSON, ROBERT, BOYLE, IAN T., and POLLOCK, DAVID. The diagnosis of parathyroid overactivity in a population of renal stone formers. *Brit. J. Surg.*, July, 1972, *59*, 517–521. (From: The Royal Infirmary, Glasgow, Scotland.)

This study was undertaken to determine the practical value of various tests in discovering primary hyperparathyroidism in a large outpatient population of renal stone formers. A total of 205 patients was screened, and the metabolic testing discovered 5 patients in whom parathyroid tumors were subsequently found and an additional patient with biochemical changes of hyperparathyroidism in whom there were contraindications to operation.

The authors recognize the value of calcium determinations, and particularly serial calcium determinations in finding patients with hyperparathyroidism, but depending upon this factor is insufficient, as the mean value of serum calcium varied only slightly in a group of stone formers as compared with a group of normal blood donors used as a control. Much time may be saved in uncovering the overactivity of the parathyroid by the use of tests of the manner in which the kidneys handle phosphate excretion.

The authors use the phosphate excretion index which compares the relationship between serum inorganic phosphorus and tubular reabsorption of phosphate. Use of this determination will indicate those individuals, among a group with hypercalcemia, who will not require exploration for possible parathyroid overactivity. Investigation of phosphate excretion will also indicate parathyroid overactivity among stone formers with primary hyperparathyroidism during those phases in which the serum calcium may be minimally elevated or may fall within the normal range.—*E. Frederick Lang, M.D.*

MOFFAT, ROBERT E., CHANG, C. H. (JOSEPH), and SLAVEN, JOHN E. Roentgen considerations in primary pulmonary artery sarcoma. *Radiology*, Aug., 1972, *104*, 283–288. (Address: C. H. J. Chang, M.D., University of Kansas Medical Center, Kansas City, Kansas 66103.)

Three additional cases of primary pulmonary artery sarcoma are reported bringing the total to 33 reported thus far in the world literature. The important features of all the reported cases are reviewed.

This disease has occurred almost twice as frequently in females. The average patient age was 51 years, ranging from 22 to 81 years. Subtle development of right heart failure of unknown cause was the most common clinical picture. Preoperative or preautopsy diagnosis was never made in any of the cases.

Pathologically, there was usually marked distention of the affected artery with obliteration of the vessel lumen. The main pulmonary artery was involved in every case. Pulmonary infarction occurred in 13 cases. Histologically, most were of the spindle-cell variety. There were 11 fibrosarcomas and 9 leiomyosarcomas.

Roentgenographically, the disease was most often characterized by a unilateral, lobulated hilar mass which followed the distribution of a pulmonary artery. The lobar or segmental arterial distribution of the pulmonary artery sarcoma should make it distinguishable from the hilar lymphadenopathy from other causes. Pulmonary angiograms in 3 cases demonstrated arterial occlusions.

Lung scanning performed in 1 of the authors' cases revealed a marked perfusion defect.

Lung scans are recommended in suspected cases.—*J. M. Stoebner, M.D.*

Beiser, G. David, Epstein, Stephen E., Stampfer, Morris, Goldstein, Robert E., Noland, Stanton P., and Levitsky, Sidney. Impairment of cardiac function in patients with pectus excavatum, with improvement after operative correction. *New England J. Med.*, Aug., 1972, *287*, 267–272. (From: Cardiology Branch, National Heart and Lung Institute, Bethesda, Md.)

Catheterization of the right heart was performed on 6 patients with pectus excavatum. The hemodynamic response to exercises with the patient supine was normal. The cardiac output during intense upright exercise was low in 2 patients and at the lower limits of normal in 1, and low normal in 2. Cardiac output and stroke-volume responses to mild upright exercise were also abnormal.

Following surgical repair, in 3 patients cardiac output during intensive upright exercise increased an average of 38 per cent. The hemodynamic response to mild upright exertion also changed to normal. No alterations occurred in response to supine exercises.—*Saul Heiser, M.D.*

Abdomen

Ring, Ernest J., Ferrucci, Joseph T., Jr., Eaton, S. Boyd, Jr., and Clements, James L. Villous adenomas of the duodenum. *Radiology*, July, 1972, *104*, 45–48. (Address: Dr. E. J. Ring, Department of Radiology, Massachusetts General Hospital, Boston, Mass. 02114.)

Villous adenomas are a relatively common well-defined pathologic entity and are found mostly in the colon and only rarely in the upper gastrointestinal tract. The tendency of these tumors to undergo malignant transformation has been well documented.

A recent review of the literature revealed reports of 82 villous adenomas in the stomach, 6 in the duodenum, 3 in the ileum, and only 2 in the jejunum.

The authors report the clinical, pathologic, and roentgenographic features of 6 additional duodenal villous adenomas.

In their series of 6 patients with histopathologically proved villous adenomas, 5 of these were primary in the duodenum and the 6th was found in the duodenal cap after having prolapsed through the pylorus. The signs and symptoms, in order of frequency, were jaundice, anemia, weight loss, nausea and vomiting. In 2 of these cases adenocarcinoma was documented. The biopsy from a third case was reported benign, but the tumor was large and unresectable and it was felt that the benign biopsy specimen resulted from sampling error.

These lesions were found with barium meal examination using fluoroscopy and compression spot filming. Hypotonic duodenography with air contrast coating of the surface of these lesions best showed the cauliflower-like appearance so characteristic of these tumors. Barium coating the interstices between the finger-like projections produced a palisaded or striated appearance similar to that seen in the villous adenomas found in the colon. The smaller lesions tended to have a nonspecific appearance and occasionally, as in the colon, the tumor presented only as a superficial warty excrescence roentgenographically simulating thickened mucosal folds.

Since the size, shape, margins, and adjacent mucosal deformity were not reliable signs to help differentiation of benign villous adenomas from those with early carcinomatous transformation, it is felt that wide local resection or even more radical excision of the lesion is the treatment of choice.—*Donald N. Dysart, M.D.*

van Langenberg, Arthur, and Ong, G. B. Carcinoma of large bowel in the young. *Brit. M. J.*, Aug., 1972, *3*, 374–376. (From: University of Hong Kong, Queen Mary Hospital, Hong Kong.)

One of the most frequent malignant diseases in the adult is cancer of the large intestine with peak incidence in the sixth decade. Fortunately, it is also one of the more favorable forms of malignancy in terms of operability and long term survival.

During a 10 year period from 1961 the authors collected 582 cases with carcinoma of the large intestine of which 21, or 4 per cent, were in young patients between the ages of 13 and 25 years. In comparison with other published series the authors feel that not only is the incidence of these tumors increasing in young adults, but also in children and adolescents. The presenting complaints are similar for patients of any age.

Forty-five per cent of the 21 cases were dead by the end of the first year and there was no 5 year survivor. The average survival was 10.2 months from the time of admission. Carcinoma of the large intestine is more malignant in the young than in the adult. The diagnosis may be delayed by natural reluctance to diagnose carcinoma in a young patient. Delay in presentation of the patient is likewise an important factor as most patients were seen first in an advanced state of the disease.

The youngest patient with carcinoma of the large intestine was recorded in 1880, when the disease was discovered in a premature infant.—*E. Frederick Lang, M.D.*

Clark, A. W., Lloyd-Mostyn, R. H., and Sadler, M. R. de C. "Ischaemic" colitis in young adults. *Brit. M. J.*, Oct., 1972, *4*, 70–72. (Address: A. W. Clark, F.R.C.S.,

Surgical Registrar, King's College Hospital, London S.E.5, England.)

Since 1963, when ischemic colitis was first described, the diagnosis, course, and possible outcome have been well established. The patients are usually over 45 years of age. The outcome varies between complete recovery and infarction of the entire intestinal wall leading eventually to stricture formation.

The authors have collected from the literature 10 cases in which the patient was younger than 42 years and add 4 of their own between the ages of 21 and 36 years.

The authors' cases were typical of ischemic colitis with left sided abdominal pain and bloody diarrhea which improved rapidly. The barium studies showed typical thumb-printing or saw tooth irregularity, and 3 of the 4 subsequently returned to an entirely normal roentgen appearance of the large intestine. One patient, the 36 year old, progressed to stricture in the upper part of the descending colon. In 3 of the patients at operation the involved segment of colon was thickened and reddened, but the blood supply appeared to be normal. No resection was carried out. In 1 of the cases the involvement was in the right half of the colon. In the additional cases reported in the literature in this age group the low incidence of stricture formation and the high frequency of the right sided lesions were notable. In most of these reported 14 cases in the young there was no obvious cause for the ischemic colitis and the symptoms were transient.

In contrast, in the older age group, cardiac disease, diabetes, rheumatoid disease, and arteriosclerosis are incriminated; the incidence of stricture is common; and the lesion is predominantly found in the region of the splenic flexure. It appears that the prognosis depends upon age.—*E. Frederick Lang, M.D.*

GENITOURINARY SYSTEM

MACEWEN, G. DEAN, WINTER, ROBERT B., and HARDY, JAMES H. Evaluation of kidney anomalies in congenital scoliosis. *J. Bone & Joint Surg.*, Oct., 1972, *54-A*, 1451–1454. (Address: G. Dean MacEwen, M.D., P. O. Box 269, Wilmington, Del. 19899.)

Because instances of serious kidney disease have been noted unexpectedly in isolated cases of congenital scoliosis, a series of consecutive patients with scoliosis and without urinary tract complaints was examined by routine intravenous urography. Two hundred and thirty-one consecutive children with congenital scoliosis (excluding myelomeningocele) were examined and the ratio of females to males was 2:1. Eighteen per cent had some urologic anomaly, and one-third of these had unilateral renal agenesis.

The incidence of the various anomalies was compared with the incidence in a series of almost 20,000 routine pediatric autopsies. There were 6.5 per cent with unilateral renal agenesis in the authors' group, compared with 0.2 per cent in the routine autopsies. A duplication anomaly was found here in 4 per cent compared with 0.7 per cent in a group of more than 50,000 routine autopsies. Renal ectopia accounted for 2.5 per cent incidence here, compared with 0.1 per cent in routine autopsies. Single instances of horseshoe kidney, medullary sponge kidney, and bladder abnormality were noted.

Some of the anomalies encountered, such as unilateral renal agenesis, make the patient susceptible to injury, infection and obstruction. Some of the anomalies found were associated with obstruction which was progressive, and treatment of this situation before it becomes symptomatic is obviously to the patient's advantage. In some of the patients in this study, treatment of the scoliosis was postponed because of the urgency of the urinary tract problem.

The authors suggest that exclusion of urinary tract anomalies in children with congenital scoliosis, regardless of the location or severity of the spinal deformity, is of considerable value.—*E. Frederick Lang, M.D.*

BISHOP, M. C., WOODS, C. G., OLIVER, D. O., LEDINGHAM, J. G. G., SMITH, R., and TIBBUTT, D. A. Effects of haemodialysis on bone in chronic renal failure. *Brit. M. J.*, Sept., 1972, *3*, 664–667. (Address: M. C. Bishop, M.B., Research Registrar, Metabolic Unit, Nuffield Orthopaedic Centre, Oxford, England.)

Quantitative histologic studies have been done on 80 sequential bone biopsies taken at yearly intervals from 37 patients with chronic renal failure on long term hemodialysis. In one group the biopsies were made before dialysis and again 1 year later. In the second group the biopsy was made between 6 months and 3 years after the beginning of dialysis. Bone was from the iliac crest and from alternate sides of the pelvis.

In this study it was found that in about half the patients bone was abnormal before the beginning of dialysis. During dialysis the mean osteoid area and the maximum number of unmineralized osteoid lamellae increased while the area of mineralized bone decreased. These changes were more pronounced in the first year of treatment than subsequently. Immobilization may be very important in this respect because some patients spent long periods in the hospital during the first year of dialysis. Four patients were subjected to parathyroidectomy with no influence on the bone loss. The authors conclude that neither loss of bone nor increased volume of unmineralized osteoid can be regarded as specific effects of long term hemodialysis, but only of advanced uremia.

Note is made of the regional variation in the incidence of bone disease occurring during dialysis, with

pain and unhealed pathologic fractures occurring commonly. These were not observed in the authors' patients in Oxford, England, and the authors suggest that unidentified factors in tap water removed by deionizers probably contribute to the osteomalacia and may be responsible for this regional variation.—*E. Frederick Lang, M.D.*

Williams, D. Innes, Fay, R., and Lillie, J. G. The functional radiology of ectopic ureterocele. *Brit. J. Urol.*, Aug., 1972, *44*, 417–433. (From: St. Peter's Hospitals and Institute of Urology and Hospital for Sick Children, Great Ormond Street, London, England.)

Ectopic ureterocele is an anomaly associated with a double upper urinary tract. The upper kidney is generally poorly functioning or nonfunctioning, and its distal ureter may prolapse producing a filling defect at the bladder base. The diagnosis may be established by intravenous urography. The nonopacified dilated abnormal ureter may be suspected by the displacement of the visualized ureter draining the lower pole producing a series of scalloped curves.

Cystography provides the principal information, demonstrating the size and position of the ureterocele, its tension and compressibility, the degree to which it is backed by firm detrusor fibers, any tendency to prolapse into the urethra and the extent to which bladder elimination is obstructed.

The filling defect caused by ectopic ureterocele is always based on the bladder outline in contrast to the usual ureterocele which appears completely outlined within the bladder shadow. Occasionally, the ectopic ureter exhibits not only ureterocele dilatation within the bladder, but a second saccular dilatation lying posterior to the urethra. This may cause stretching out and partial obstruction of the supramontanal segment in the male, or the entire urethra in the female. The presence of the second posturethral sac is only clearly demonstrated when it is filled with opaque medium, and occasionally this does occur by reflux from the urethra. In other circumstances it can be surmised from the urethral deformity, sometimes clinically in the female by the presence of a pseudoprolapse alongside the urethral meatus. The degree of compressibility of the ureterocele is determined on the studies made before and during micturition.

A prolapsed ureterocele may become necrotic and spontaneously rupture. Simple instrumentation may lead to rupture also before a diagnosis is made. Such ruptures usually produce an irregular defect just outside the outline of the bladder with the free edge occasionally forming an irregular filling defect within the bladder shadow.—*Saul Heiser, M.D.*

Makker, Sudesh P., Tucker, Arthur S., Izant, Robert J., Jr., and Heymann, Walter. Nonobstructive hydronephrosis and hydroureter associated with peritonitis. *New England J. Med.*, Sept., 1972, *287*, 535–537. (Address: Dr. W. Heymann, Rainbow Babies and Childrens Hospital, 2103 Adelbert Road, Cleveland, Ohio 44106.)

Hydronephrosis and hydroureter may be associated with peritonitis, probably based on the disturbance of peristaltic activity of the upper urinary tracts.

Three cases are reported with peritonitis associated with the dilated upper urinary tracts. One of these was primary and the other 2 associated with ruptured appendix. In all 3 cases the nonobstructive dilatation disappeared spontaneously within 4 to 20 months after onset.

There was no evidence of urinary tract infections. All cases had an associated ileus of the bowel.—*Saul Heiser, M.D.*

RADIATION THERAPY

Penn, C. R. H., and Hope-Stone, H. F. The role of radiotherapy in the management of malignant thymoma. *Brit. J. Surg.*, July, 1972, *59*, 533–539. (From: Department of Radiotherapy, The London Hospital, London, England.)

A series of 18 cases of malignant thymoma referred for radiation therapy during a 21 year period is reviewed. All had histologically proved malignant thymoma and all received radiotherapy. In 15 cases radiotherapy was used as part of the original management of the disease. In 2 it was used for recurrence following surgery alone, and in 1 age and poor general condition indicated palliative irradiation.

The age at presentation ranged between 19 and 69 years. All patients had lesions detectable on plain roentgenograms; 4 had palpable lymph nodes; distant pulmonary metastasis occurred in 1 patient; and another patient developed multiple bone metastases $7\frac{1}{2}$ years after presentation.

Histologically, 2 were classified granulomatous thymoma and the others were invasive thymoma. Of these, 1 was epithelial, 6 were lymphocytic, and 6 were mixed. Of the latter 2 groups, 4 presented with myasthenia. Fifteen cases were submitted to thoracotomy, and in 8 macroscopically complete removal was achieved. In 2 removal was known to be incomplete, and in the other 5 only a biopsy was performed.

Four patients received at least 4,000 rads in the megavoltage range in 20 treatments over 28 days and another 3 received the same dose with conventional deep roentgen therapy. The remaining 8 were treated palliatively with between 2,000 and 3,500 rads.

The only serious complication was 1 patient with pneumonitis. Some patients experienced mild pneu-

monitis which responded to prednisone. Mediastinitis and pericarditis did not occur; temporary spinal cord damage may have occurred in 1 patient with complete recovery and no residual neurologic deficit.

The 7 cases who received radical radiotherapy were all alive 3 years following treatment. Five could be followed 5 years and were all alive. One died 6½ years following treatment. Three were followed for 10 years and all are alive without recurrence. In this small group there is shown no advantage in complete surgical excision when there is subsequent radical irradiation. Since the response of late recurrence after radical surgery to irradiation is so poor, it would seem reasonable to suggest that all cases of infiltrating tumors could with advantage be referred for postoperative radiotherapy, even if surgery is complete. Locally inoperable cases should perhaps be given a chance likewise to respond to radical irradiation.—*E. Frederick Lang, M.D.*

JONES, STEPHEN E., KAPLAN, HENRY S., and ROSENBERG, SAUL A. Non-Hodgkin's lymphomas: III. Preliminary results of radiotherapy and a proposal for new clinical trials. *Radiology*, June, 1972, *103*, 657–662. (From: Departments of Medicine and Radiology, Stanford University Medical Center, Stanford, Calif.)

Presented is a preliminary report of the results of radiotherapy in 2 dissimilar groups of patients with localized non-Hodgkin's lymphoma classified according to the criteria proposed by Rappaport *et al.* Four hundred and seventy-four previously untreated patients seen between 1960 and 1970 were classified in this way and the results of radiotherapy analyzed. Staging was by the Rye classification regarding extent of associated lymph node disease.

Some patients received high-dose involved-field treatment, while others were given high-dose extended-field irradiation which included adjacent noninvolved regions. A tumor dose of at least 3,000 rads in 3 weeks was given; most patients received 4,400 rads in 4 weeks.

Survival and risk of relapse were analyzed in each category, also taking into account the stage of disease. Patients with localized diffuse histiocytic lymphoma had a median survival of 13 months with a high risk of relapse within 1 year of treatment. Patients with nodular mixed histiocytic-lymphocytic or nodular lymphocytic poorly differentiated lymphoma had a median survival of 80 months and tended to have a late relapse pattern. Relapse was both to lymphatic and extralymphatic sites.

It was thought that some of these patients might be "cured" in view of the high probability of relapse in the first year after therapy and the small risk of late relapse. This conclusion was not drawn in the nodular group with a relatively constant and significantly high risk of relapse several years after initial radiotherapy.

A new clinical trial was started in July, 1971, to try to evolve a more effective therapy for these patients utilizing concepts established in the treatment of Hodgkin's disease: (1) high dose total lymphoid therapy can be tolerated; (2) aggressive combination chemotherapy appears capable of inducing sustained remission; and (3) high dose lymphoid irradiation can be effectively combined with chemotherapy.

Evaluation, therapy, and follow-up will be a team effort. Unless medically contraindicated, exploratory laparotomy is to be performed on the first 50 patients to assess its value. It is planned to give 4,400 rads per field in 4 weeks by megavoltage therapy. In more advanced cases combination chemotherapy will also be used. This will consist of cyclophosphamide, vincristine and prednisone with half of the patients receiving bleomycin as a fourth drug.

Much time and effort will be required to establish the effectiveness of this trial, but it is hoped that it will result in more effective therapy for patients with non-Hodgkin's lymphoma.—*M. J. Sedlmeir, M.D.*

NOBLER, MYRON P. Efficacy of a perineal teletherapy portal in the management of vulvar and vaginal cancer. *Radiology*, May, 1972, *103*, 393–397. (From: Department of Radiation Therapy, Beth Israel Medical Center, New York, N. Y.)

It is a common belief that lesions arising in the perineum cannot be treated with external irradiation directly because the anatomic site "does not tolerate irradiation to any extent." It has also been stated that "supervoltage external irradiation has no place in the treatment of lesions of the vulva and adjacent perineal structures." However, the author has established a successful treatment technique for lesions of the vulva and vagina using teletherapy.

Patients with cancer of the vulva and vagina are selected for treatment, regardless of cell type, when their lesions are: too large for interstitial implantation; deeply infiltrating; multiple masses; producing fistulae; and/or the patient is not a candidate for surgery or has metastatic disease.

The treatment technique is described and 6 case histories are reported.

Isodose curves of a typical patient show the highly desirable dose distribution resulting in maximum lethal effect in the tumor and significant sparing of the bladder and rectum.

Illustrations in color of 2 cases, which show the lesions before, during, and after treatment clearly demonstrate the value of this therapeutic approach.

In the past 3 years, 6 patients were successfully treated by direct perineal portal external teletherapy irradiation. It is stressed that cancericidal doses

(5,000–7,000 rads) can completely control cancer of the vulva and vagina (local recurrence did not occur in a single instance) and still be well tolerated.—*Paul M. Kroening, M.D.*

Monson, Kenneth J., Brand, William N., and Boggs, Joseph D. Results of small-field irradiation of apparent solitary metastasis from Wilms's tumor. *Radiology*, July, 1972, *104*, 157–160. (Address: K. J. Monson, M.D., Department of Radiotherapy, Chicago Wesley Memorial Hospital, 250 East Superior Street, Chicago, Ill. 60611.)

Pulmonary metastases from Wilms's tumor should be treated with a curative aim. Although dactinomycin reduces the instances of recurrences of pulmonary metastases, approximately 57 per cent of all children with Wilms's tumor will have pulmonary metastases. Currently the management of the disease consists of combined therapy: dactinomycin; whole lung irradiation; and, in selected cases, surgery.

This study is an analysis of such a combined approach except that smaller radiation fields were utilized. This was done in hopes of reducing the morbidity.

Nineteen patients with roentgenographic evidence of Wilms's tumor metastases to the lungs were treated at Children's Hospital in Chicago, Illinois, from January, 1964 through December, 1968. All except 1, were treated with a 250 kv. constant potential roentgen-ray machine with a 1 mm. Cu plus 1 mm. Al filter. Most doses were between 1,000 r and 1,200 r midplane, delivered in 5 to 11 days. The 1 exception was treated at another institution with a megavoltage beam.

Dactinomycin was administered daily for 5 days and repeated at 3 month intervals over a period of 1 to 2 years (dose averaged 15 μg./kg. daily).

Thirteen of the 19 patients appeared to have solitary lung lesions and were treated with small field irradiation. Six of these were retreated for new lung lesions.

Four of the 13 had surgery following irradiation because of persistent lesions. Two of these had histologic evidence of persistent disease. Six of the 19 patients were treated with whole lung irradiation because of bilateral disease. In the authors' series, small field irradiation gave a survival rate of 38 per cent. This is increased to 45 per cent, if the patients initially treated at another hospital are omitted. Others report 67 per cent to 80 per cent 2 year survival with whole lung irradiation.

Pulmonary metastases from Wilms's tumor are most frequently multiple, despite an initial apparent solitary presentation. Six of 19 patients presented with roentgenologic evidence of multiple metastases, while 13 had an apparently solitary presentation. In only 5 of these 13 patients was the lesion solitary. Eight patients initially treated for solitary metastasis eventually died despite additional treatment to the lung.

These data support the use of whole lung irradiation combined with dactinomycin for the treatment of pulmonary metastases from Wilms's tumor. There is at present no way to recognize those few instances of true solitary pulmonary metastases which can be cured by irradiating less than the entire lung.—*W. O. Havens, M.D.*

Sim, Franklin H., Cupps, Roger E., Dahlin, David C., and Ivins, John C. Postradiation sarcoma of bone. *J. Bone & Joint Surg.*, Oct., 1972, *54-A*, 1479–1489. (Address: Franklin H. Sim, M.D., 200 First Street, S.W., Rochester, Minn. 55901.)

Osteitis, bone necrosis, growth disturbance, and pathologic fracture may occur following irradiation of fields including bone. Neoplasm has been reported in irradiated tissues, but postradiation sarcoma in bone is the least common. A definite relationship between exposure to radiant energy and development of sarcomas has been established in experimental animals, but the authors emphasize that there is no absolute proof that ionizing radiation caused the bone sarcomas in humans. The circumstantial evidence, however, is compelling. Approximately 150 cases of sarcoma arising in bone following irradiation have been recorded. Previously 21 cases from the Mayo Clinic have been reported; the present series reports an additional 34 cases.

In 18 patients the sarcoma developed in apparently normal bone which was included in the field for irradiation of other lesions. Six of these lesions were uterine and 5 were malignant. Three more were carcinoma of the breast. The other patients were irradiated for skin lesions, brain tumor, retroperitoneal sarcoma, and other miscellaneous problems. Of the 18, 10 were clearly suffering from a malignant disease. Among these patients the latent period between the administration of therapeutic irradiation and the development of the osseous sarcoma varied between 4 and 27 years.

The other 16 patients were treated for osseous lesions and of these 8 were histologically verified as benign lesions. Four of these were giant cell tumors and 2 were aneurysmal bone cysts. Two of the other 8 were probably giant cell tumors, 2 were possibly osteochondromas, and all of this second group of 8 were unverified. The latent period varied between 5 and 42 years, with the longest interval occurring in a 46 year old patient who developed a sarcoma in the maxilla after external irradiation and radium used in treating a proved fibrous dysplasia of the right maxilla.

Most of the sarcomas which developed were osteogenic sarcomas, although there were several fibrosarcomas. The only other lesions which developed

were 1 Ewing's sarcoma of the scapula and 1 chondrosarcoma in the humerus.

The length of the latent period is apparently not related to whether radiation was given in infancy or adulthood. The outlook after the development of the postradiation sarcoma is poor and the average survival is 1.14 years. There were only 2 long term survivors. The incidence of sarcomas in the thoracic cage following intensive therapy for breast carcinoma or in the pelvis after irradiation of uterine carcinoma is low, and the explanation for this has not been forthcoming. It has been suggested that postradiation sarcomas which developed in normal bone within the radiation therapy portal are frequently considered to be metastatic lesions.

The relationship of the tissue dose of radiation to subsequent development of sarcoma may be very important. The dosages reported in the literature are from the orthovoltage era and it is anticipated that the increased dose of supervoltage equipment with lower doses to bone will lead to decreased incidence of sarcoma after therapy. Most of the patients in this group were treated at institutions other than the Mayo Clinic and records were not available. Most of the group did show skin or osseous changes indicative of excessive radiation.

The authors suggest that irradiation of benign bone tumors should be discouraged unless the tumors are unresectable, and in addition, that, once a patient has received radiation therapy for a benign osseous lesion, follow-up should never cease.—*E. Frederick Lang, M.D.*

FARR, G. H., and HUVOS, A. G. Juxtacortical osteogenic sarcoma: an analysis of fourteen cases. *J. Bone & Joint Surg.*, Sept., 1972, *54-A*, 1205–1216. (From: Memorial Hospital for Cancer and Allied Diseases, New York, N. Y.)

Fourteen cases with juxtacortical osteogenic sarcoma seen at the Memorial Hospital for Cancer and Allied Diseases were reviewed. The pathologic features and clinical behavior divided the patients into 3 groups.

In the first group were 5 patients with classical juxtacortical osteogenic sarcoma. Microscopically, there were new bone trabeculae surrounded by a single layer of osteoblasts, with dense, well vascularized fibrous tissue interspersed. Most of these presented with a dense, lobulated mass, 5–10 cm. in dimensions, in the lower femur. The tumor may or may not be separated from the cortex by a narrow radiolucent zone and there is a peripheral, noncalcified density. A large lesion may encircle the bone. One of these classic patients presented with a multiloculated, osteolytic lesion, and in another the lesion resembled an osteochondroma. These patients did well with local excision of the tumor or primary amputation.

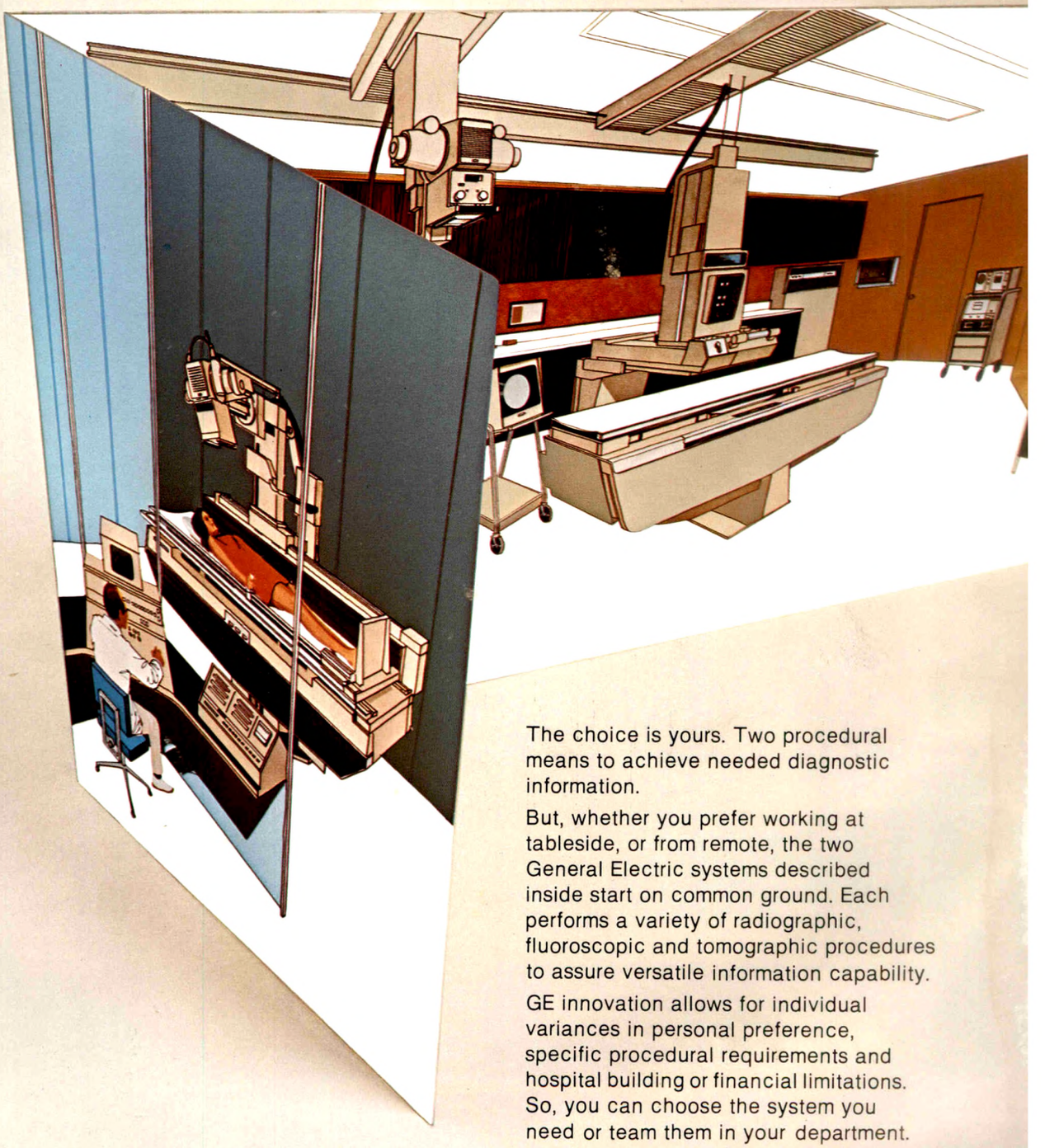
A second group of 4 patients presented significant histologic variation from the classic description. There were some cellular pleomorphism and much cartilage formation. The roentgen appearance of 1 of these was the usual juxtacortical osteogenic sarcoma, but the other 3 suggested periosteal osteogenic sarcoma, a sclerosing lesion, or myositis ossificans. This group, likewise, has done well clinically.

In the third group of 5 patients there was likewise significant histologic variation. Marked cellular pleomorphism was encountered and some exhibited little osteoid. This group presented with higher mitotic rates and some presented features of chondrosarcoma. The roentgen appearance suggested osteogenic sarcoma arising outside the bone in many, and the authors question the unqualified designation of these lesions as juxtacortical osteogenic sarcomas, since this might lead to optimism. All 5 of these patients in the third group died of their disease.

In all groups there were recurrences, but in the first group eventual cure resulted from ablative surgery. Local recurrences with metastasis and rapid growth characterized the third group. Laboratory studies did not aid in the differentiation. The authors feel that histologic study should permit clearcut differentiation and reliable prognostic classification.—*E. Frederick Lang, M.D.*

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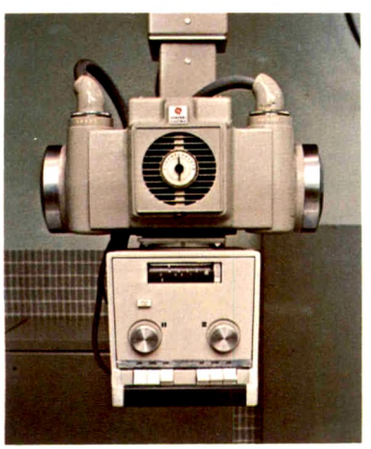
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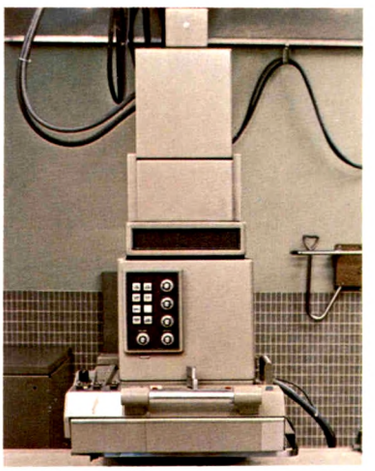
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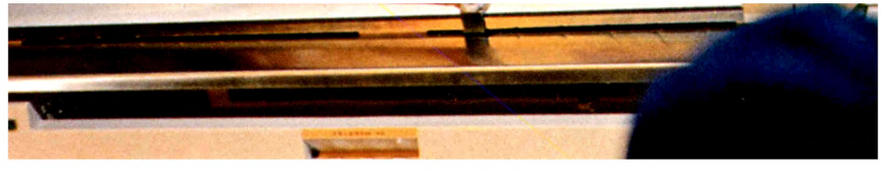
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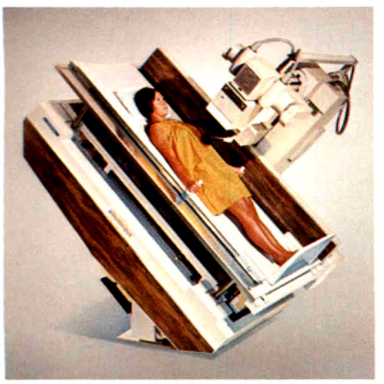


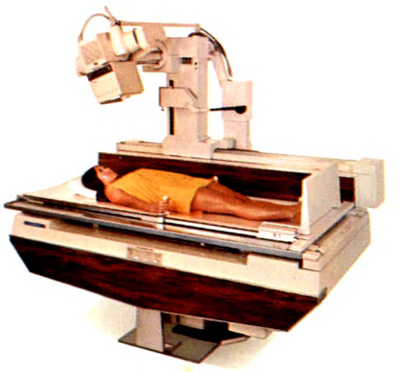
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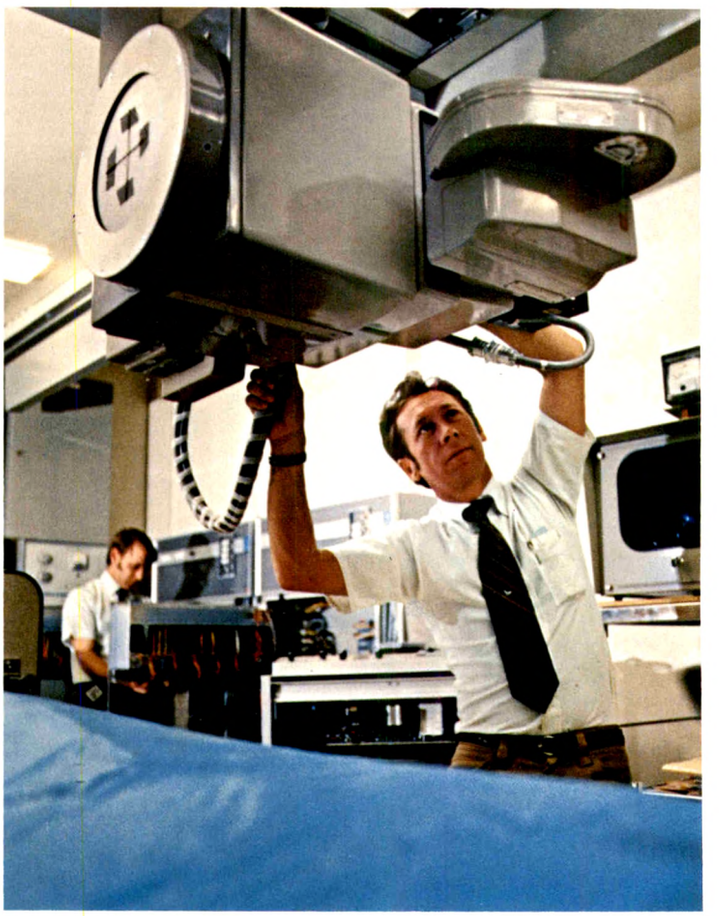
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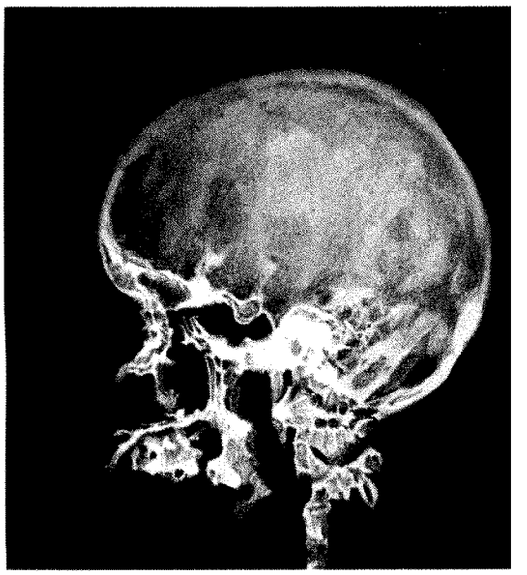
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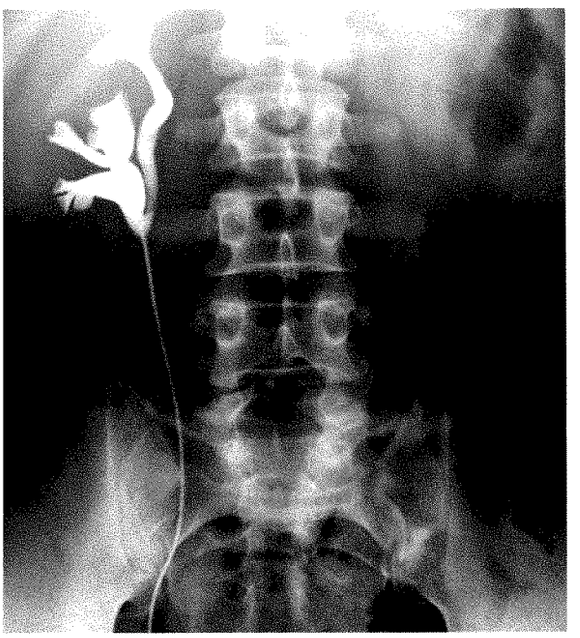
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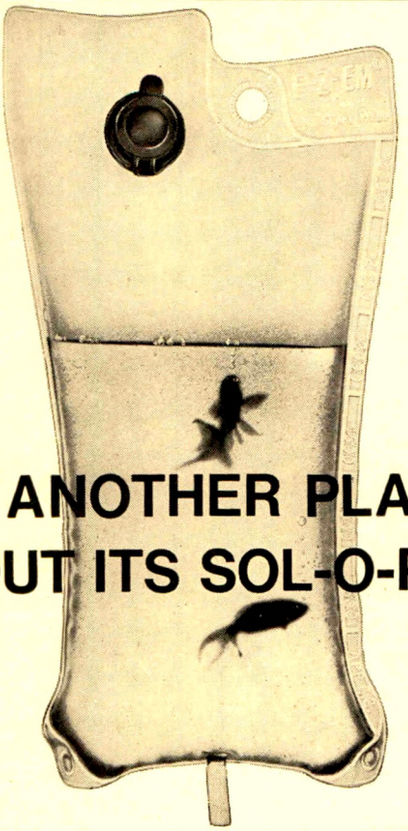
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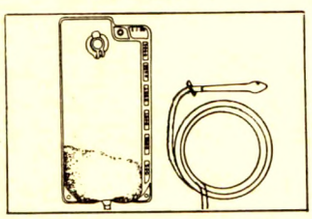
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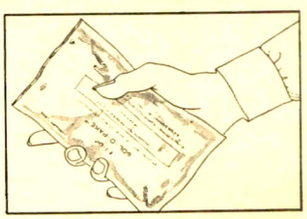
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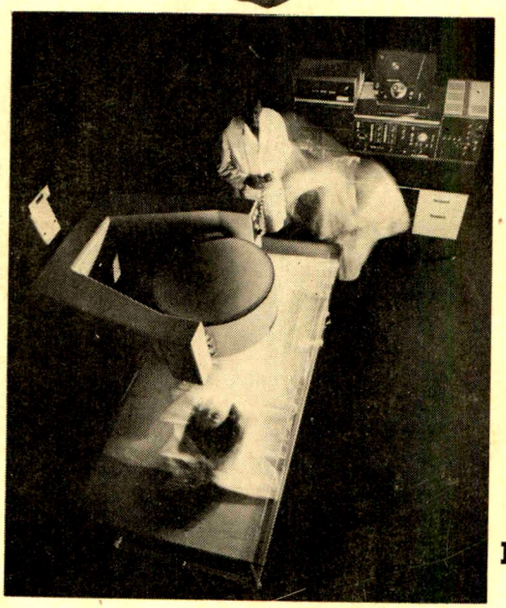
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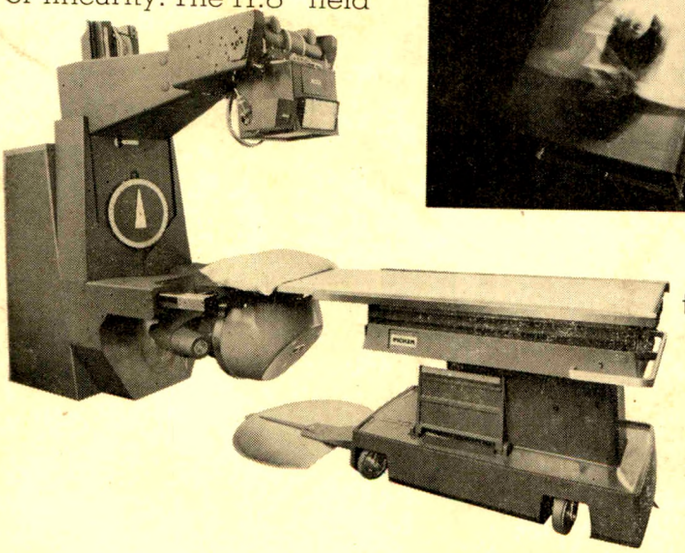
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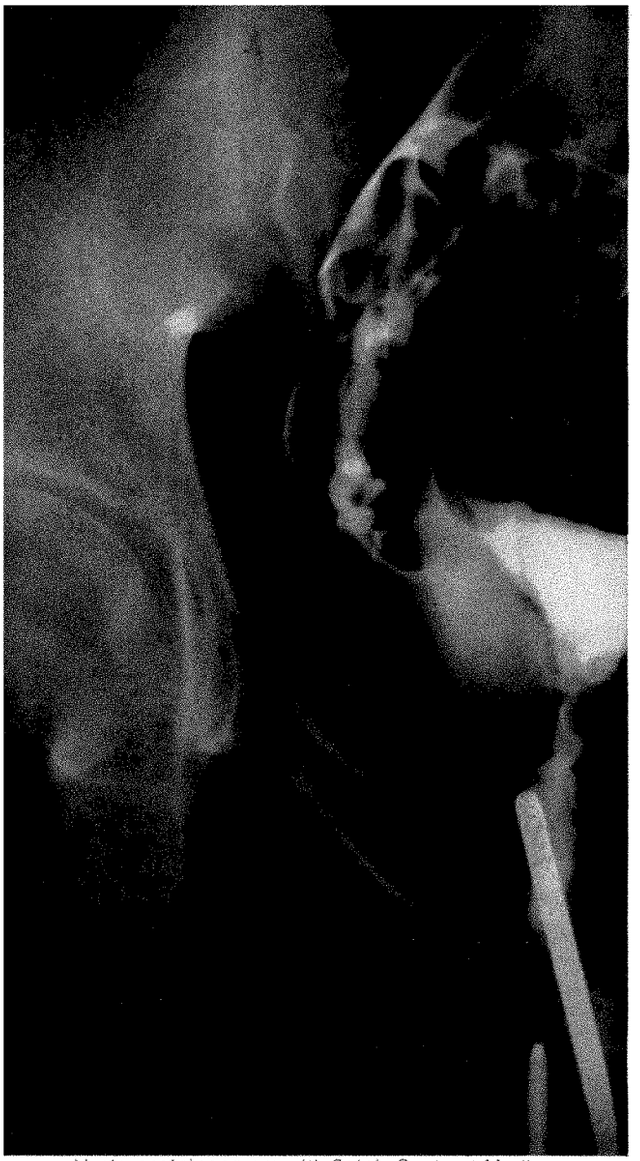
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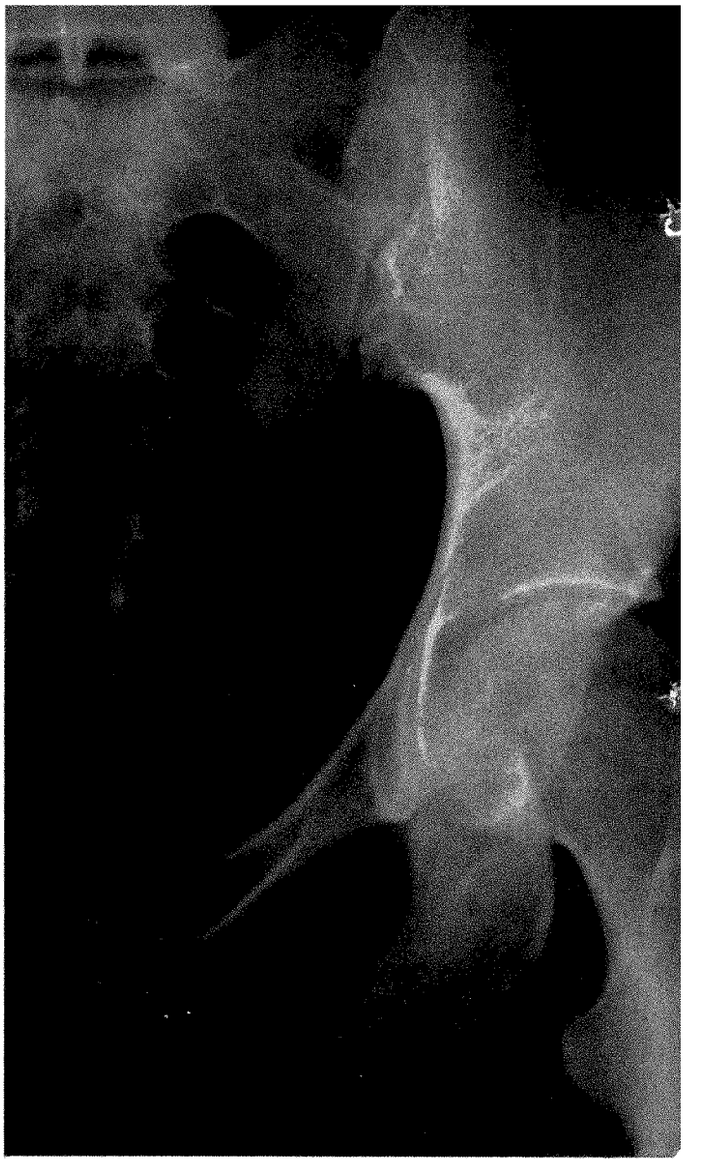
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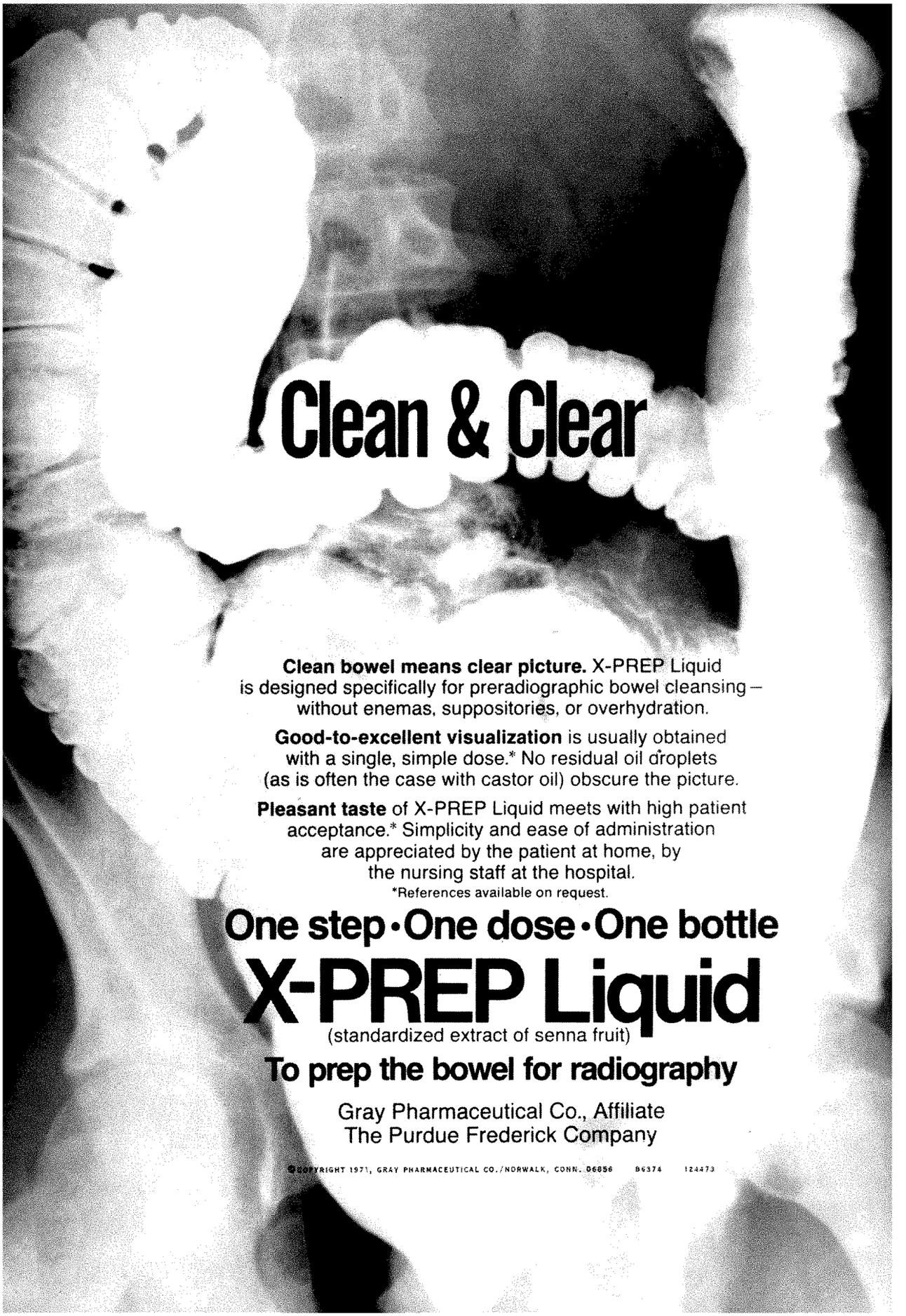
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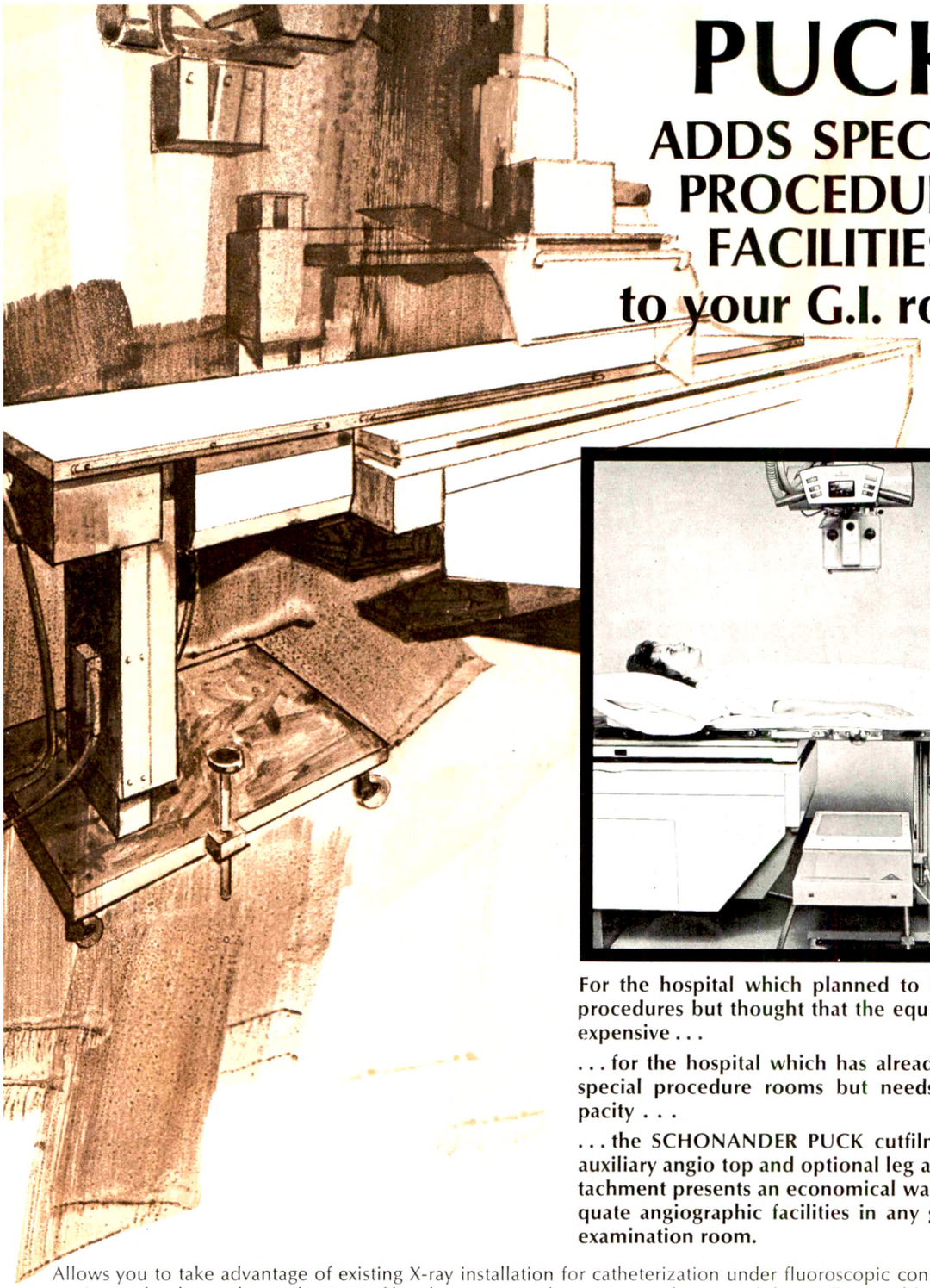
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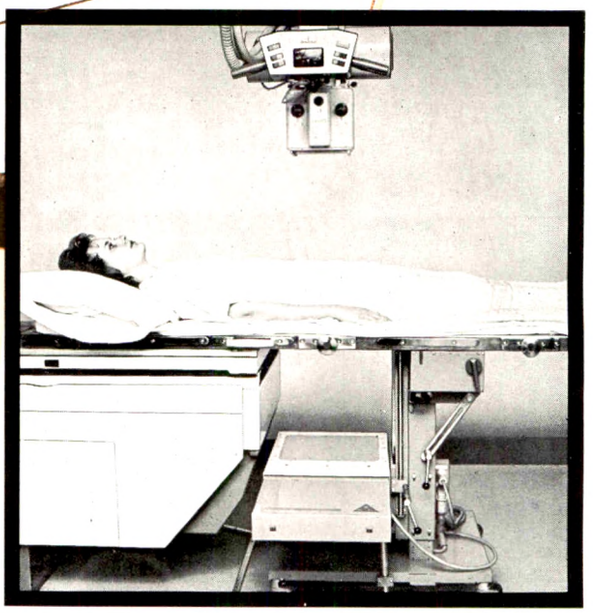
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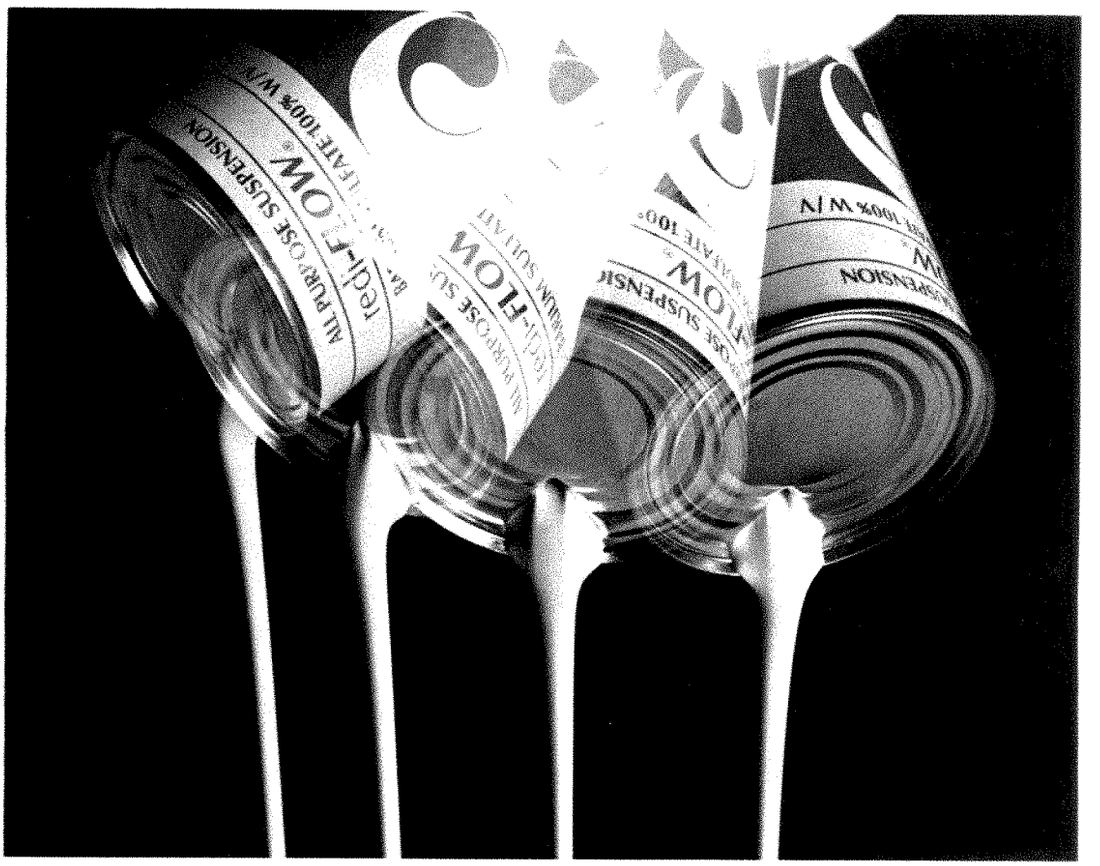
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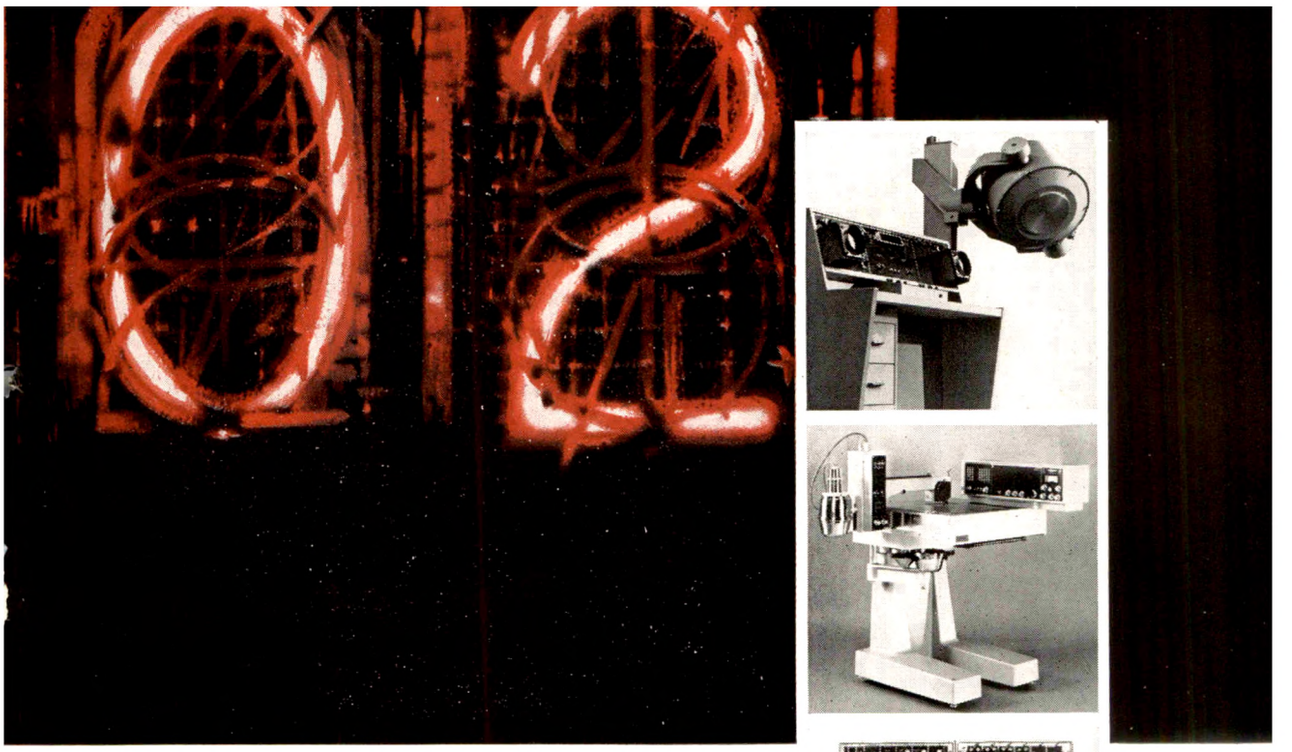


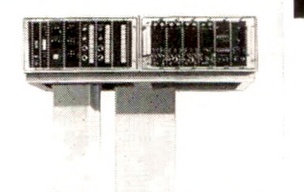
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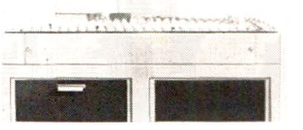


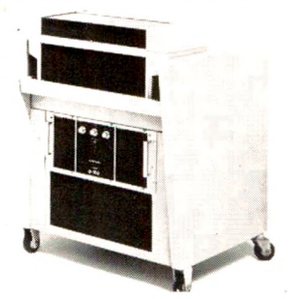
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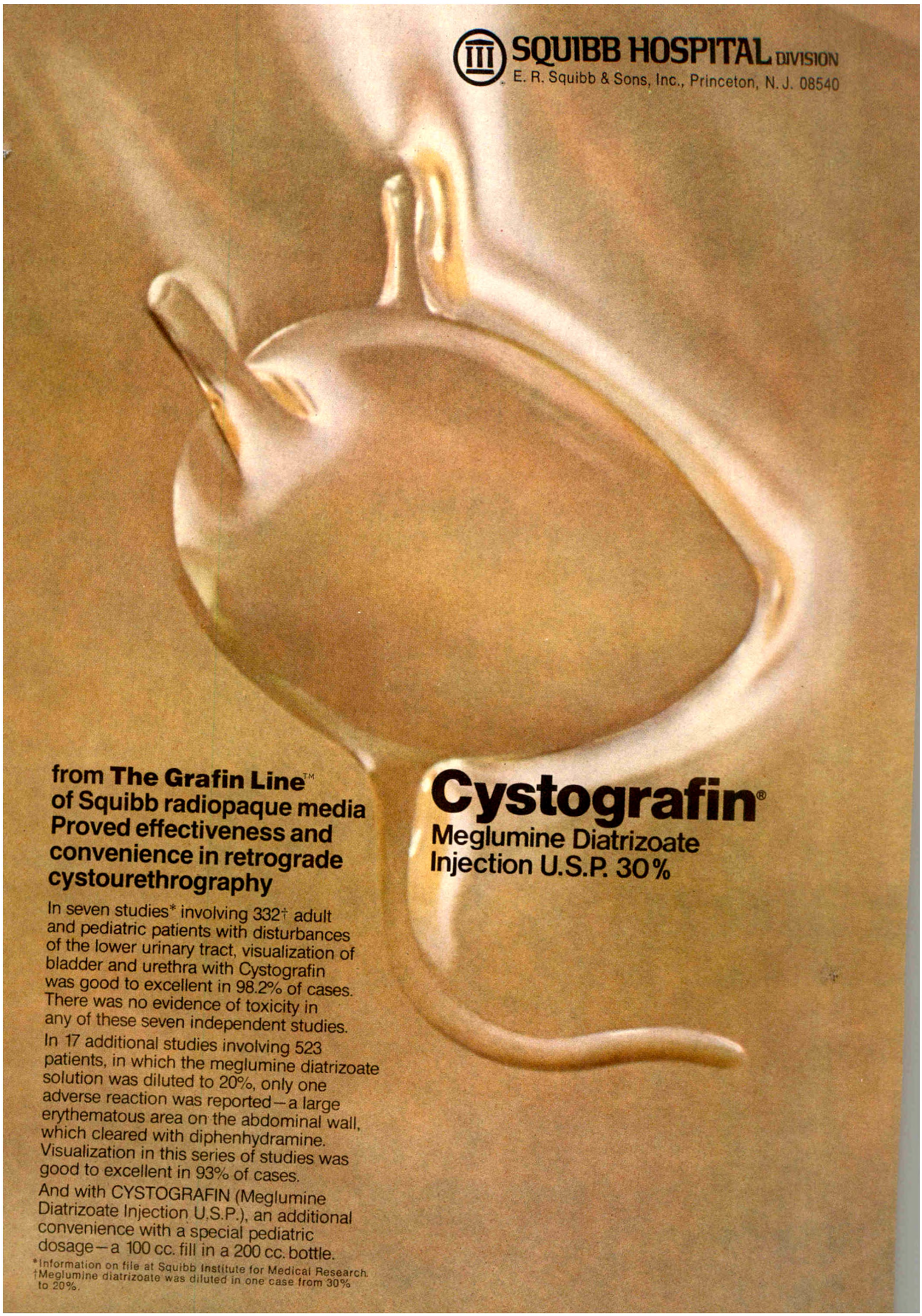
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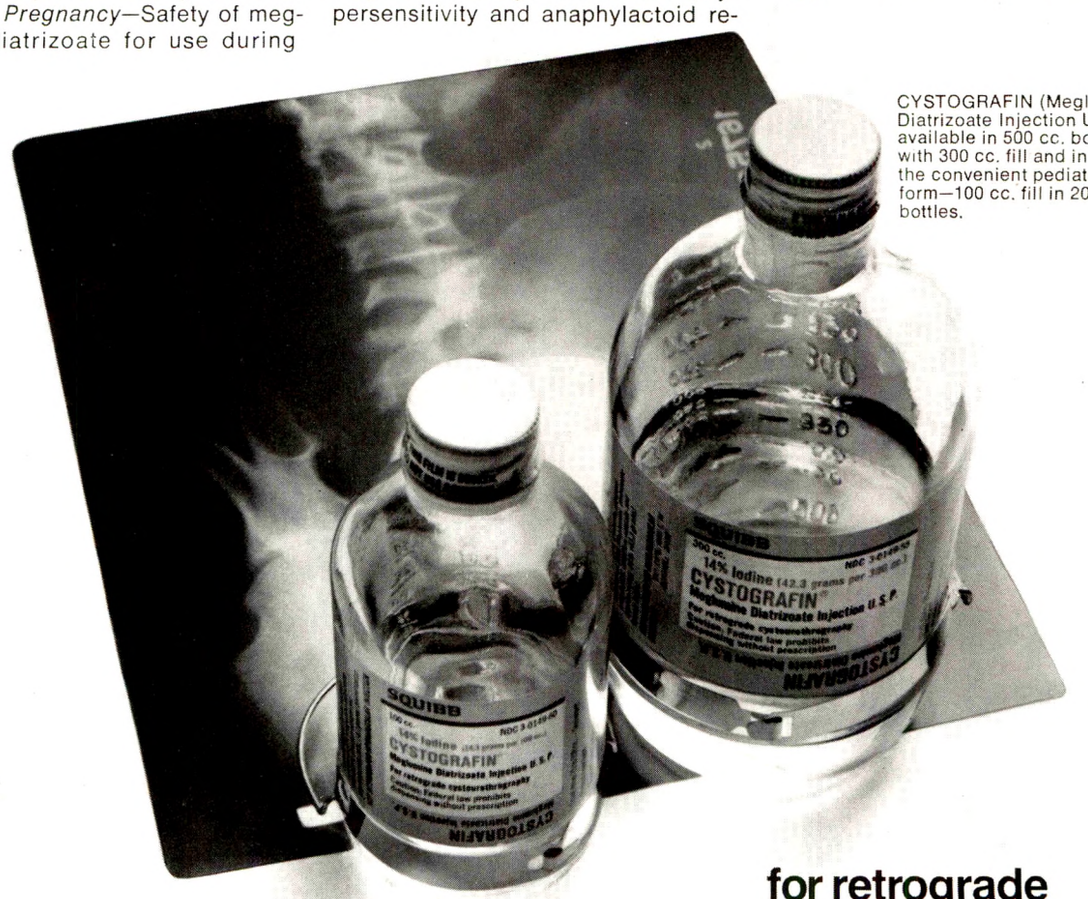
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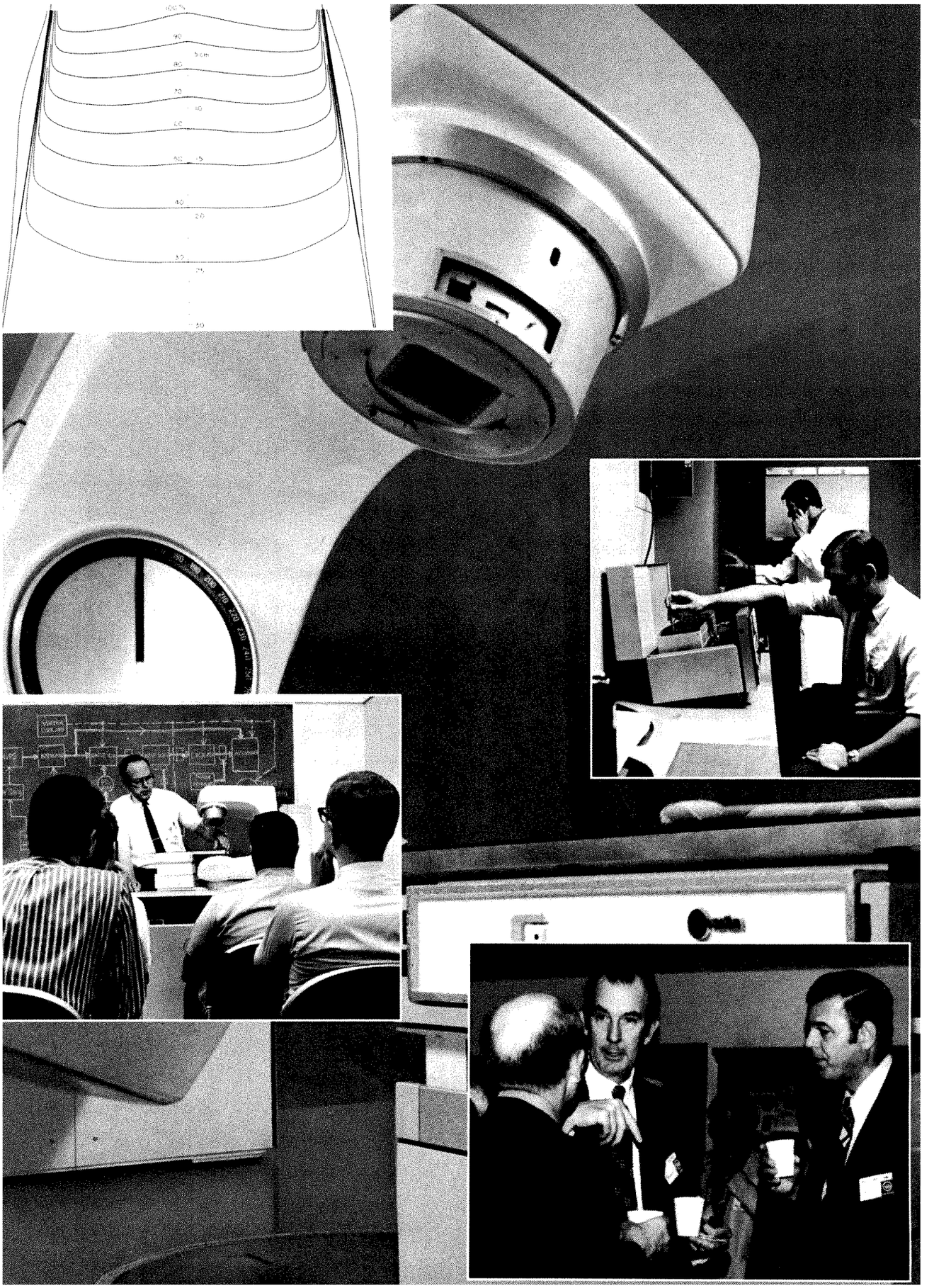
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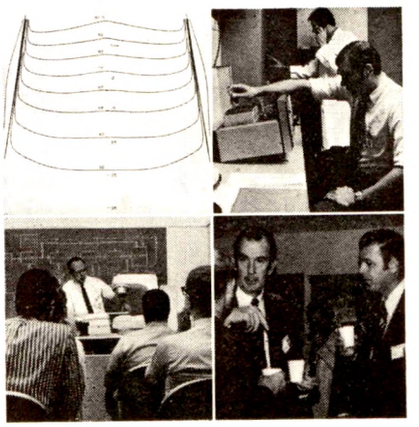
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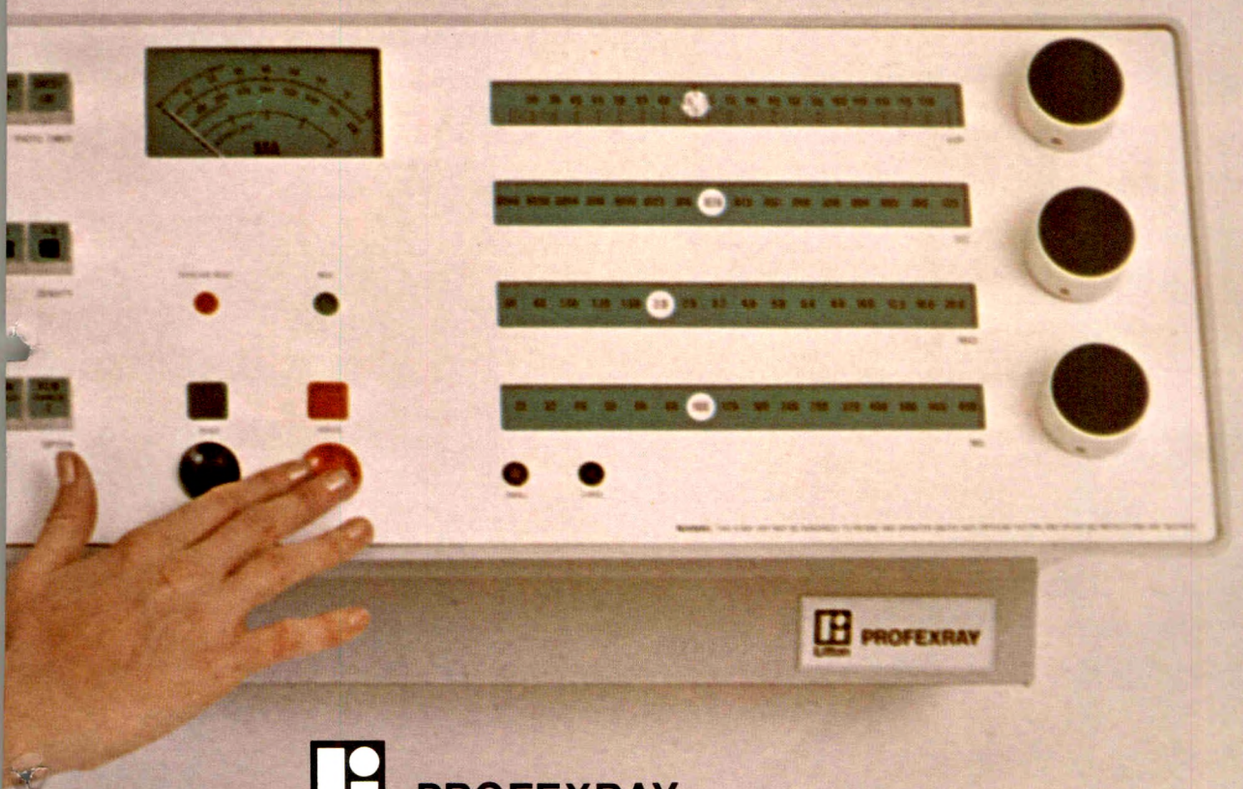
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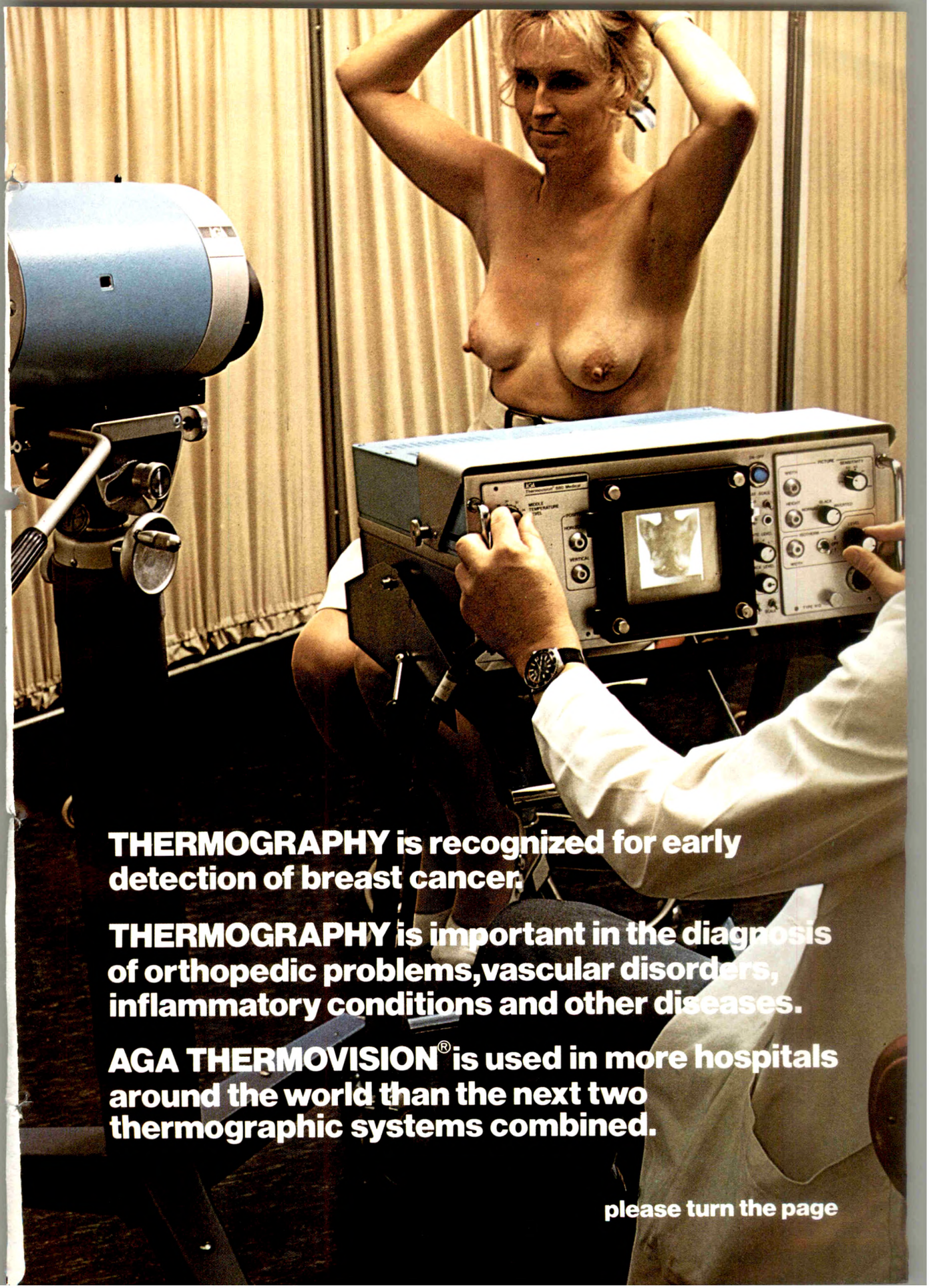
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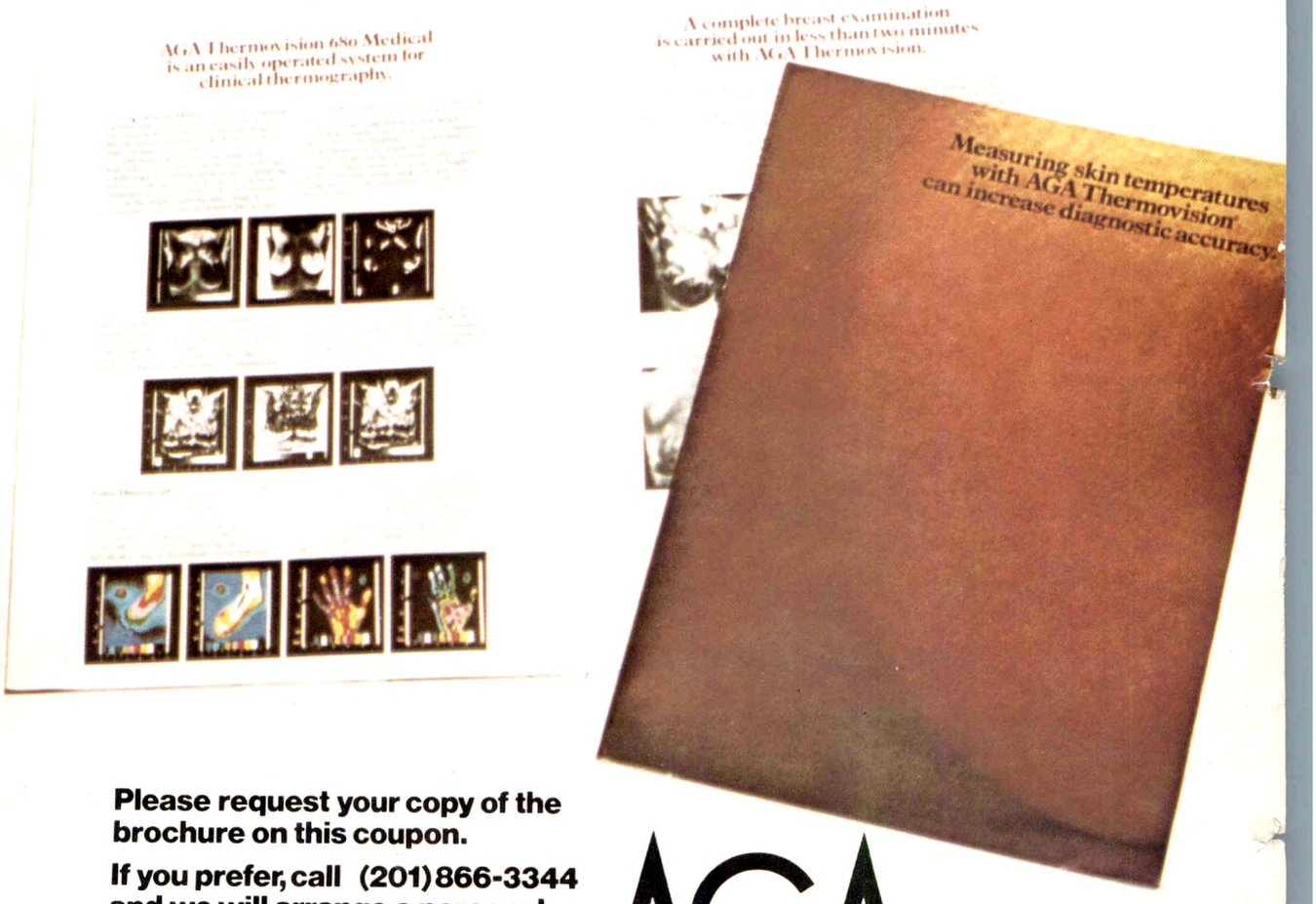
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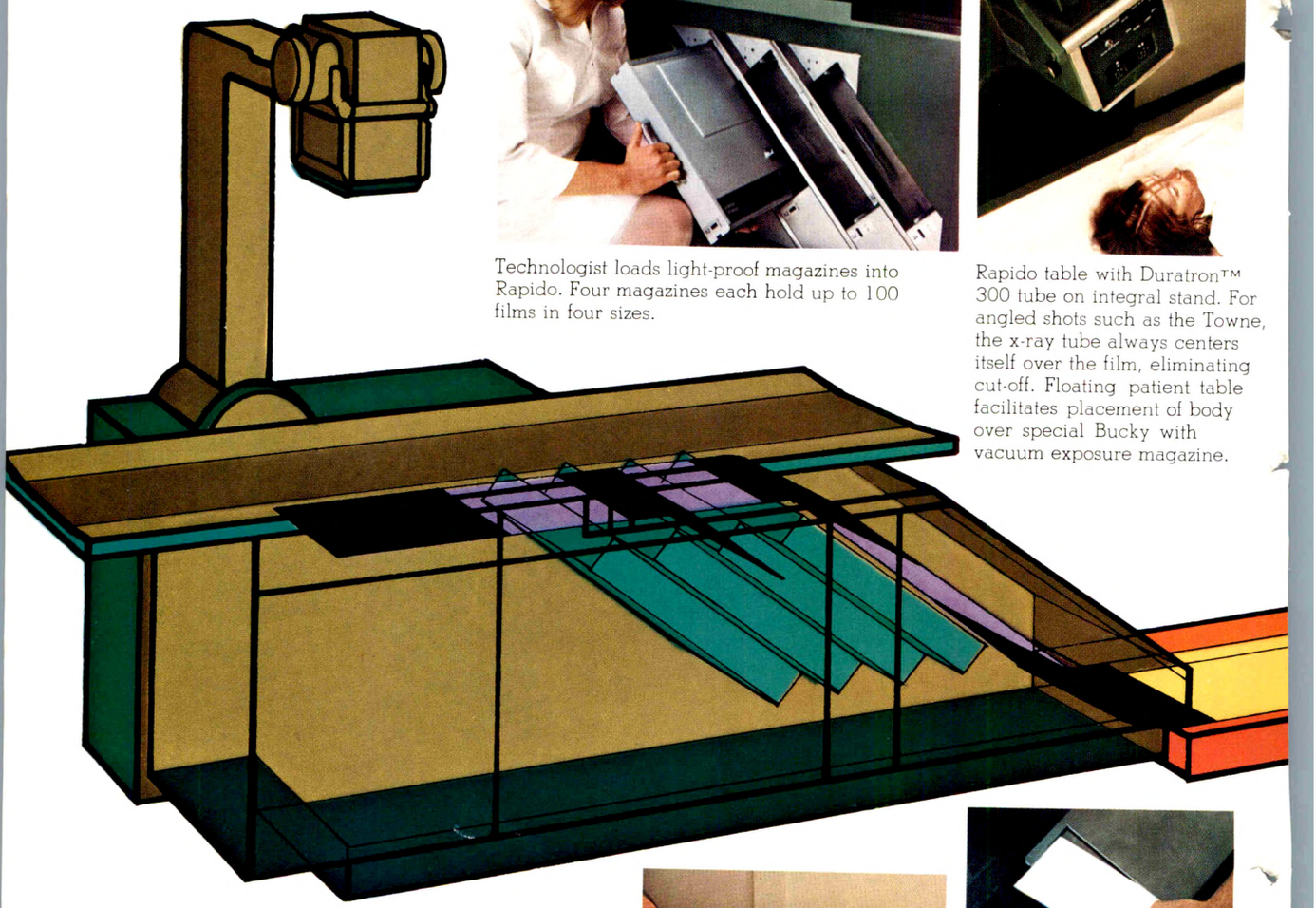
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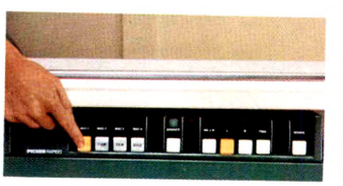


Technologist loads light-proof magazines into Rapido. Four magazines each hold up to 100 films in four sizes.



Rapido table with Duratron™ 300 tube on integral stand. For angled shots such as the Towne, the x-ray tube always centers itself over the film, eliminating cut-off. Floating patient table facilitates placement of body over special Bucky with vacuum exposure magazine.



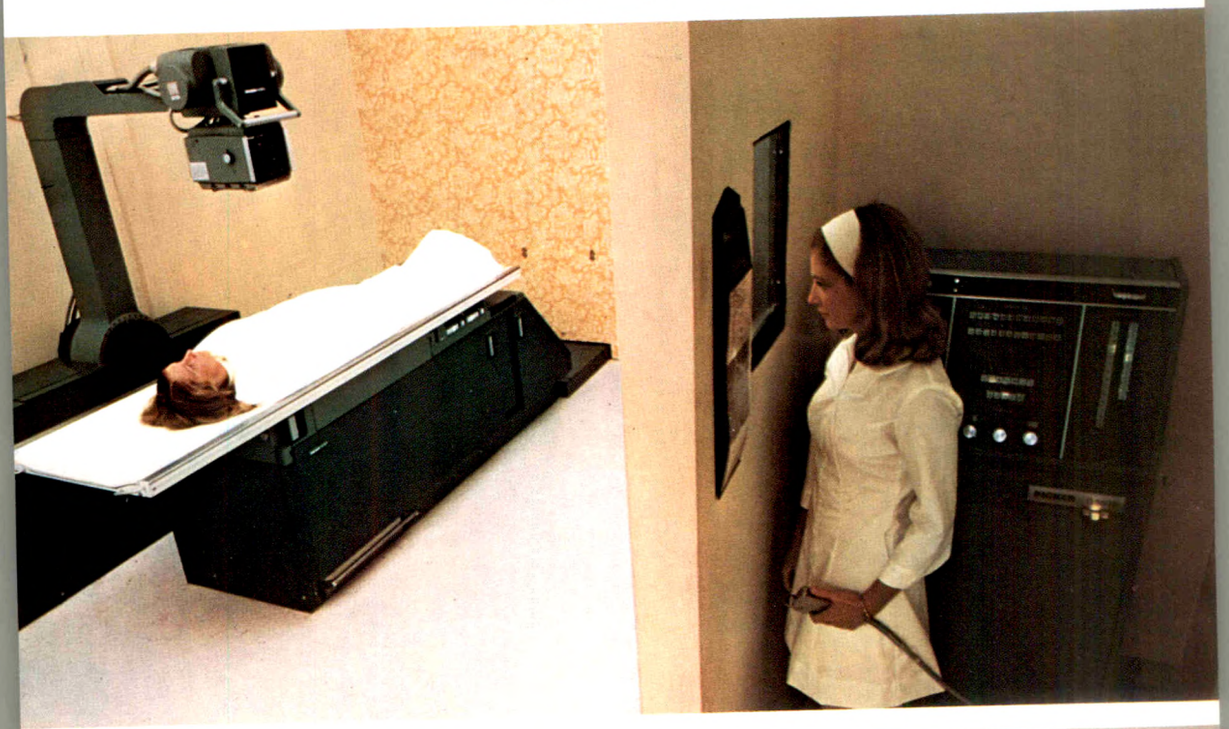




Appropriate film size is push-button selected; after exposure film moves automatically to Rap-X film conveyor system. Inserting patient's ID card permits exposure and identifies film. Eliminates extra darkroom work, minimizes identification errors, complies with medical-legal requirements.

Photos posed by professional models. Rapido system photos courtesy of the Radiological Department, Duke University Medical Center.

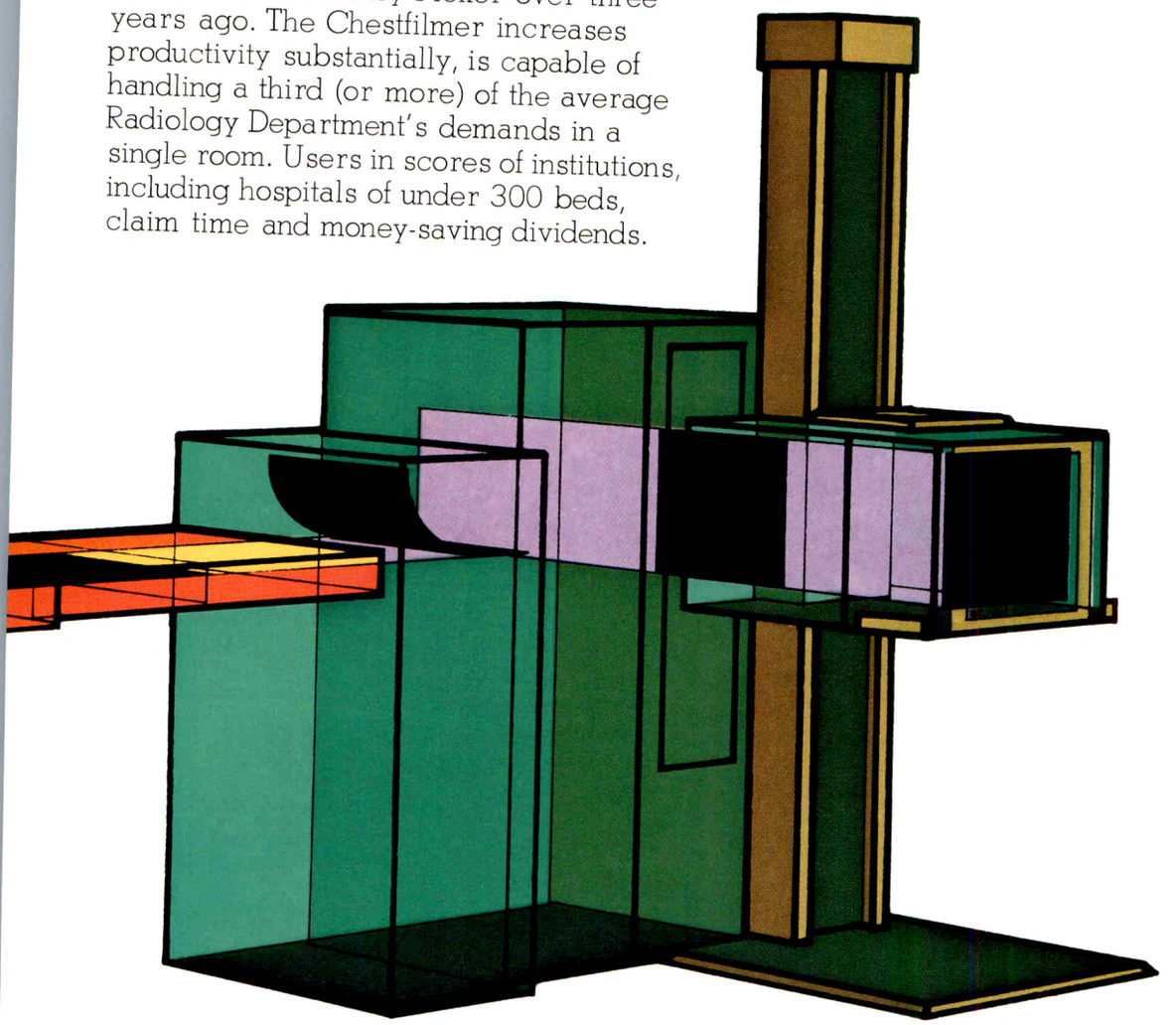
Technologist remotely controls Rapido which feeds film into through-wall Rap-X film transport system.



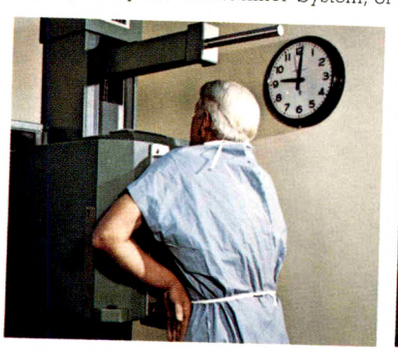


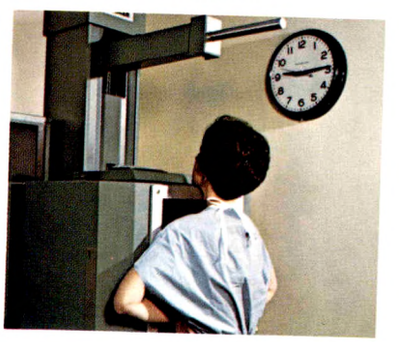
Radiologist retrieves film from Diplomat processor for viewing within an average time, from exposure, of about 120 seconds, depending on length of conveying system. Improved diagnostic image quality with Cassetteless Radiography minimizes retakes.

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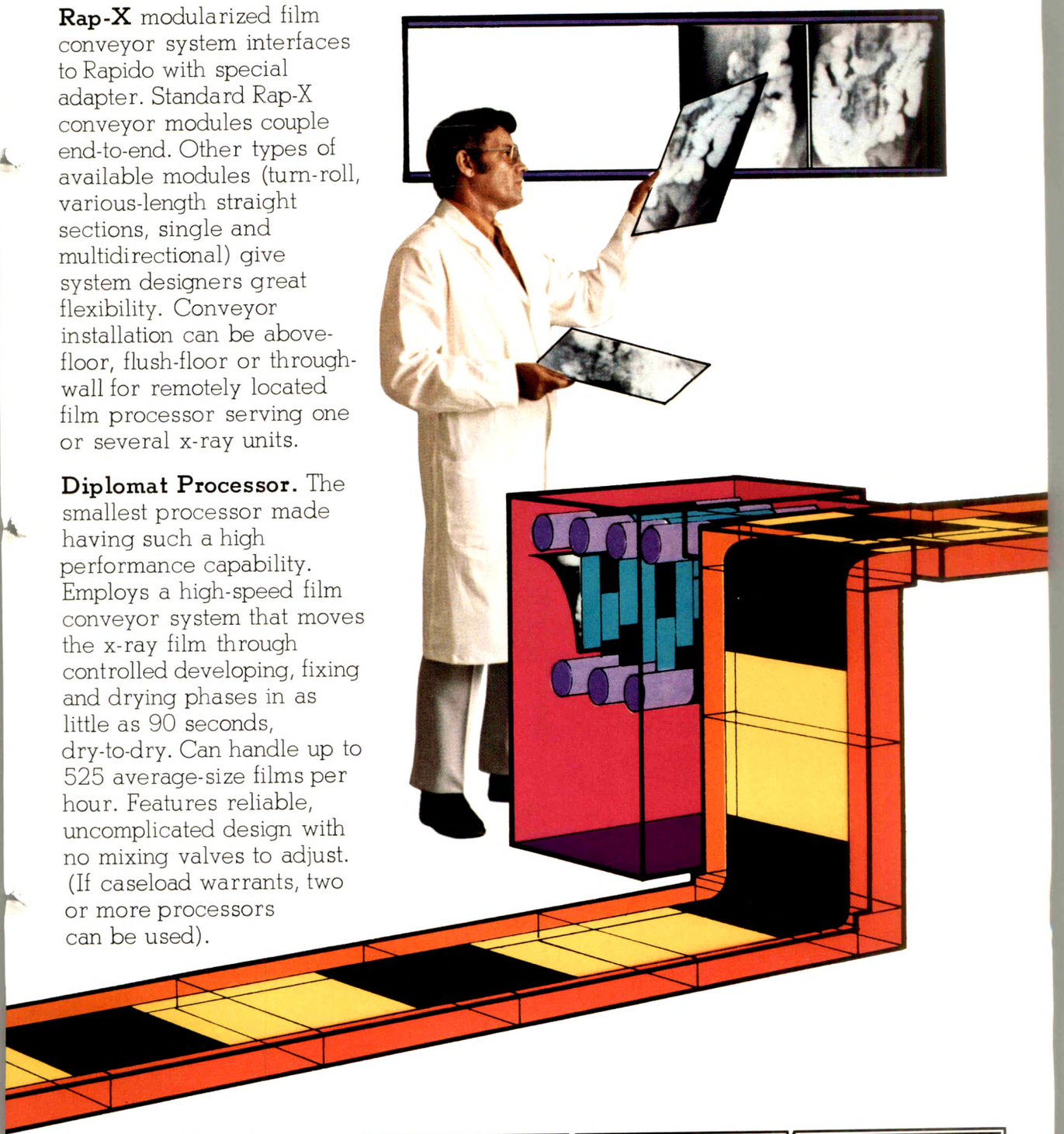
A picture of productivity. Ten patients can be x-rayed within a 15-minute time span by the Chestfilmer System, or in 20 minutes with Rapido.





Rap-X modularized film conveyor system interfaces to Rapido with special adapter. Standard Rap-X conveyor modules couple end-to-end. Other types of available modules (turn-roll, various-length straight sections, single and multidirectional) give system designers great flexibility. Conveyor installation can be above-floor, flush-floor or through-wall for remotely located film processor serving one or several x-ray units.

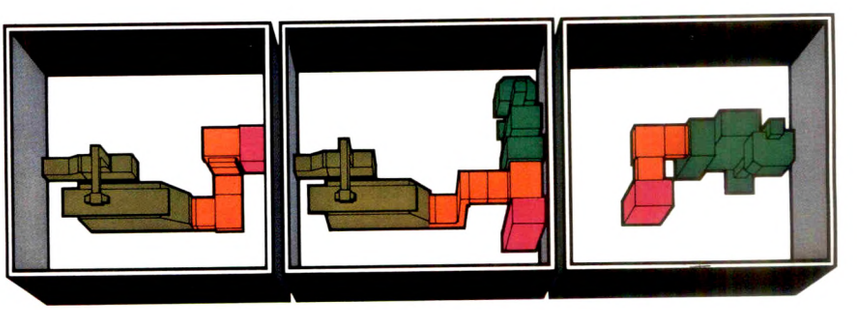
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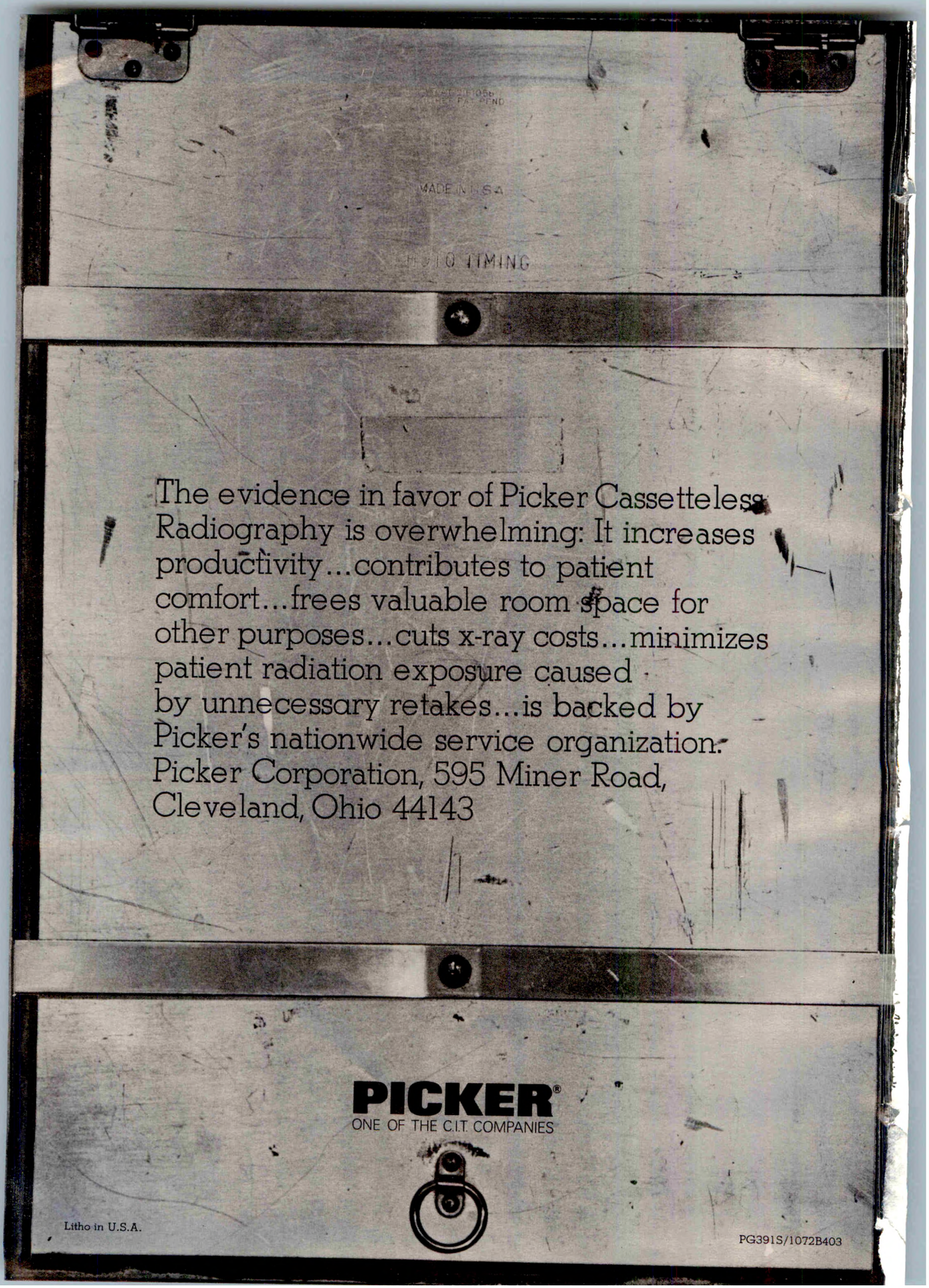


Typical cassetteless installation employing Rapido, Rap-X film conveying system and a single Diplomat processor.

Cassetteless system of Rapido and Automatic Chestfilmer with Rap-X conveyor feeding into a Diplomat processor.

Automatic Chestfilmer System with Rap-X film conveyor system and Diplomat automatic processor.





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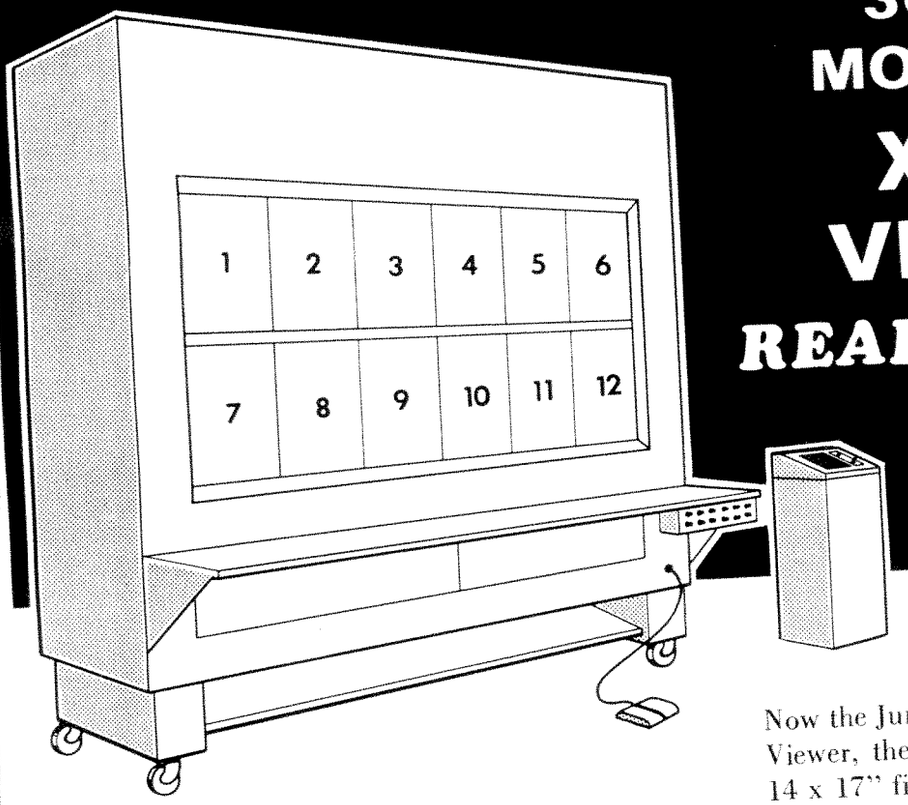
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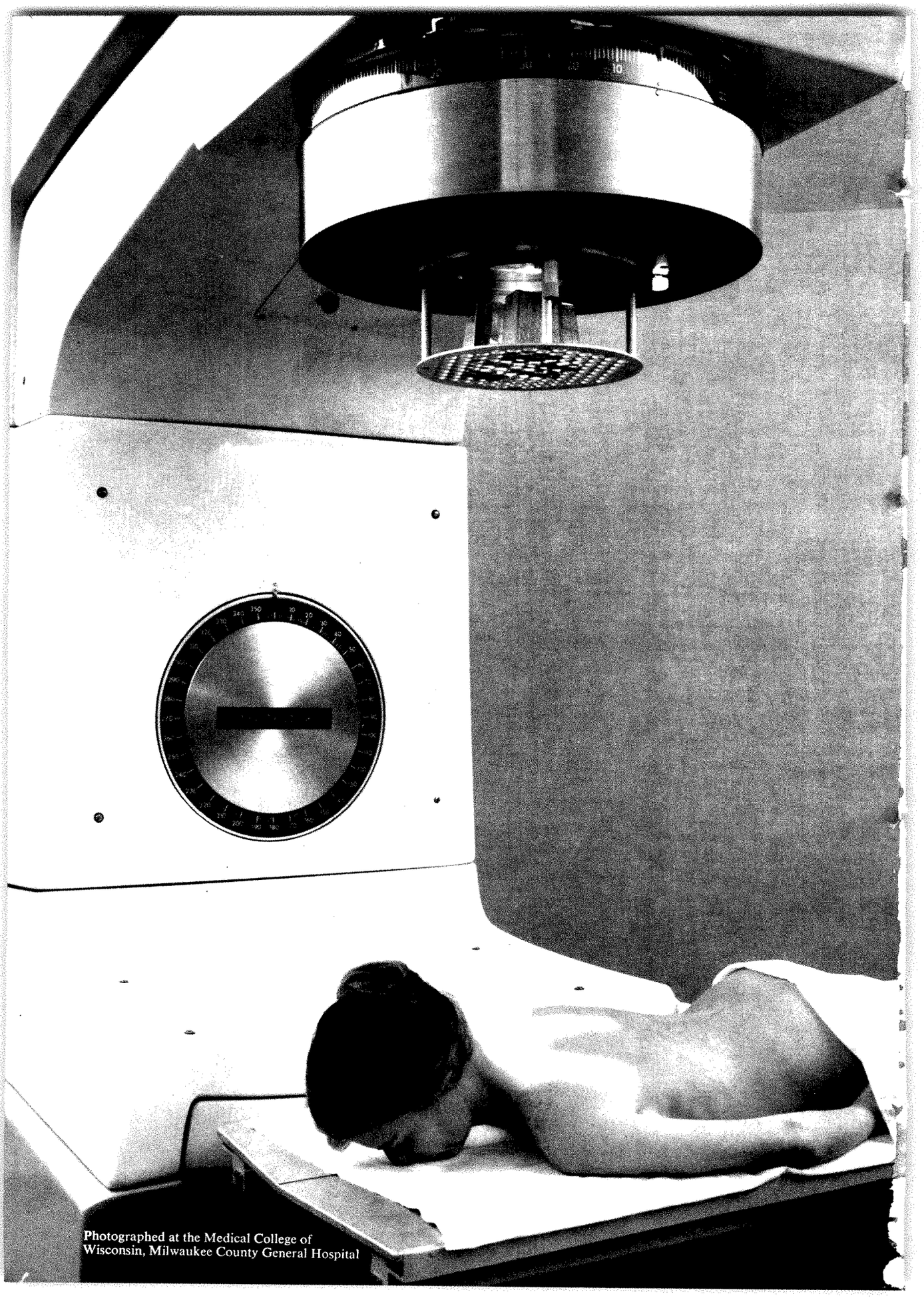
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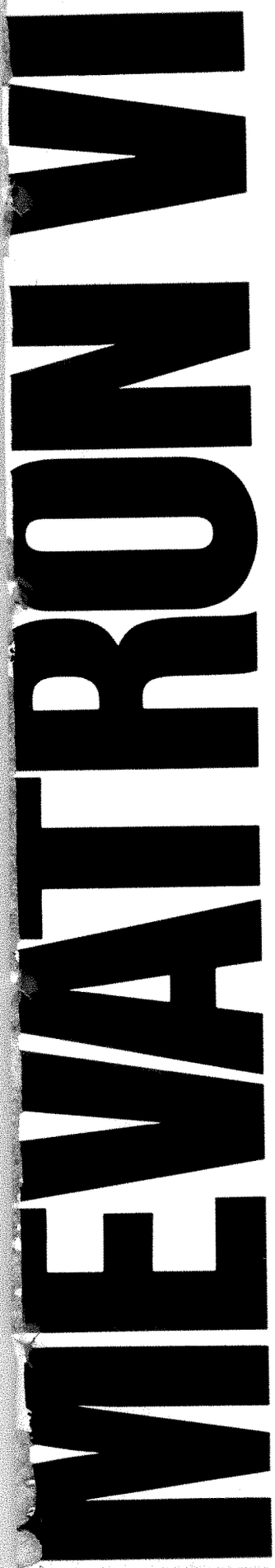
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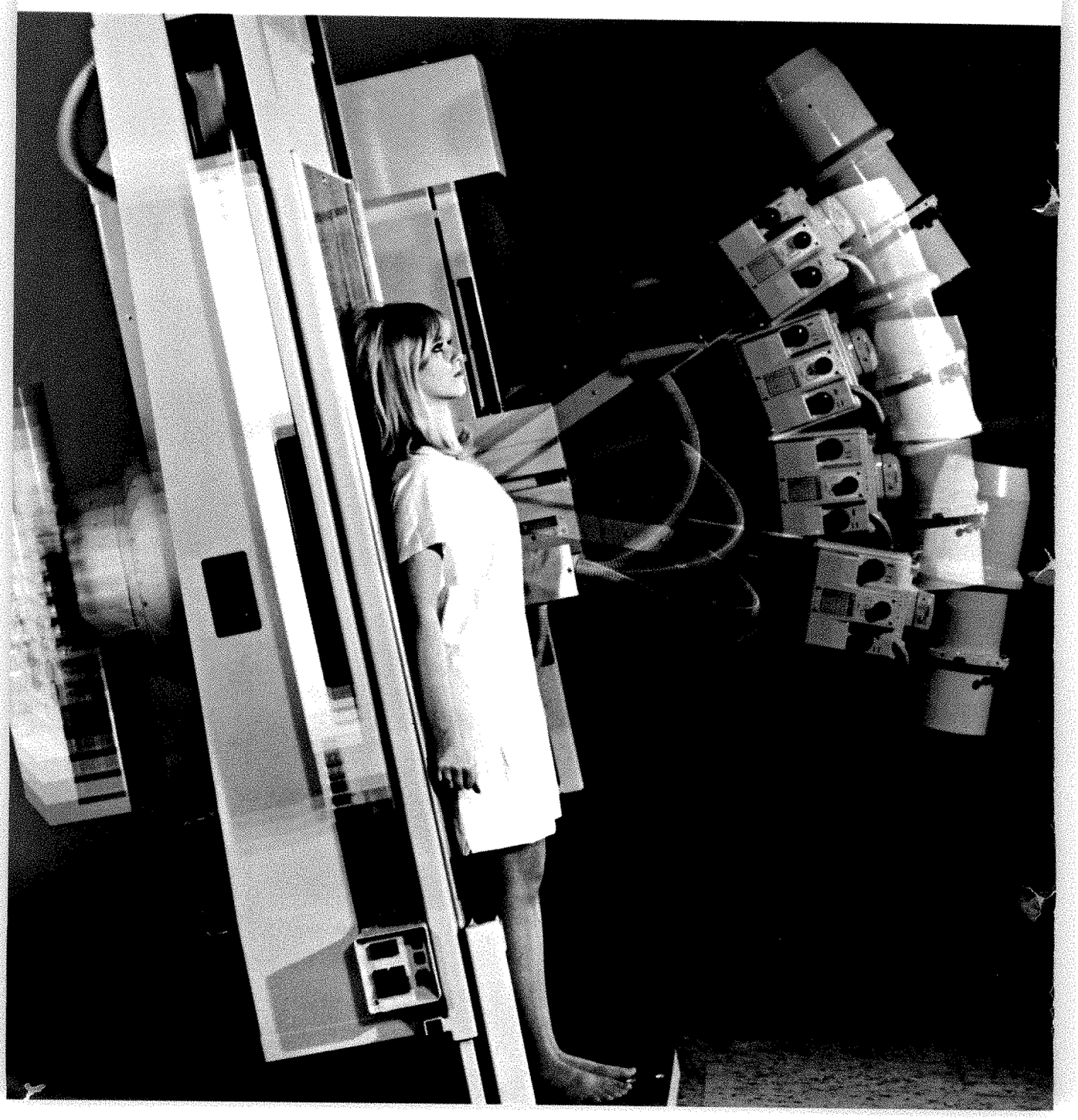
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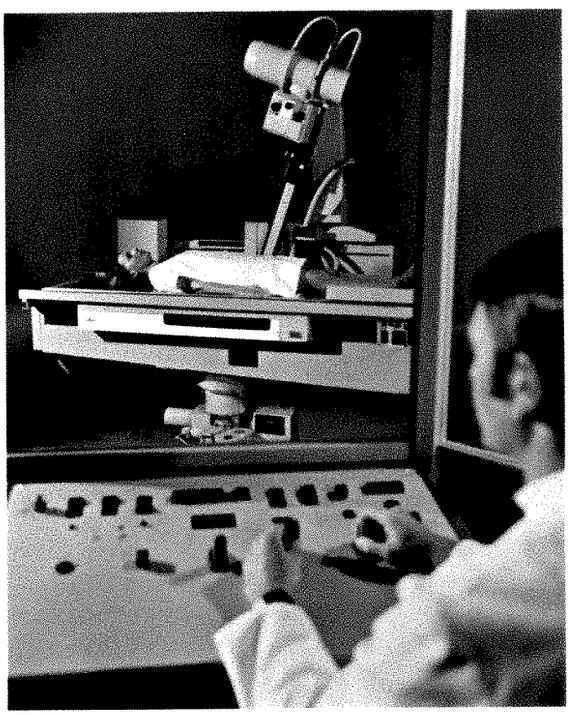
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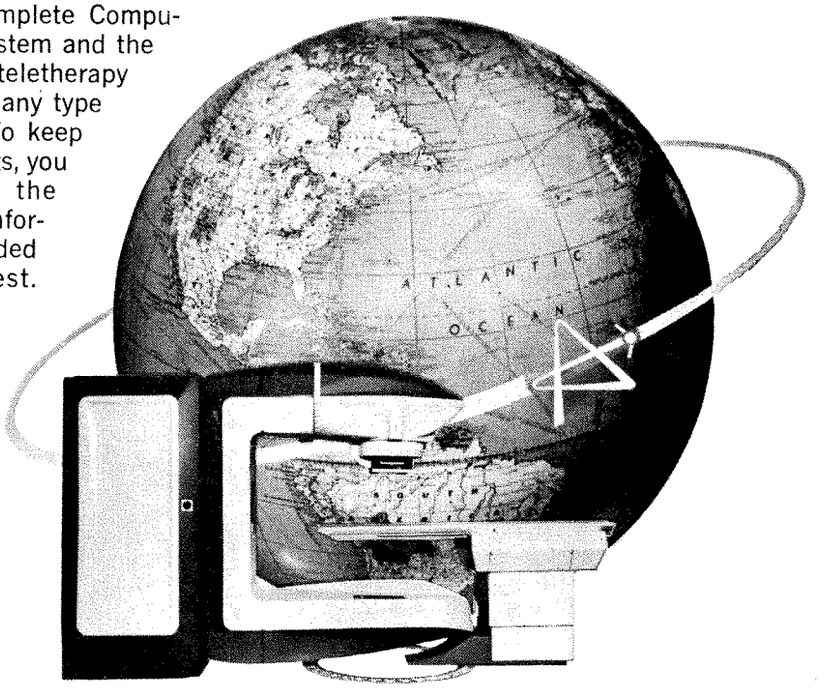


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VOL. 117 FEBRUARY, 1973 No. 2

SLIDING HIATAL HERNIA: THE NEED FOR REDEFINITION*

By BERNARD S. WOLF, M.D.
NEW YORK, NEW YORK

IT IS becoming quite popular to state that severe recurring heartburn due to gastroesophageal reflux may and does occur frequently in the absence of a sliding hiatal hernia on the basis of "primary incompetence of the gastric cardia."[4,8,11,12,14,19,21,23,24,26] It is suggested that the presence of a sliding hernia is irrelevant to the problem of reflux and that the only abnormality of significance is an incompetent intrinsic lower esophageal sphincter. The occurrence of an incompetent sphincter in association with a sliding hernia would then be coincidental and not pathogenetically related. One reason for this belief is the well-known observation that patients with obvious sliding hernias usually do not have severe heartburn, while patients with no apparent hernial sac may have intractable heartburn. If this thesis is correct, the demonstration of a hernia roentgenologically would have little relevance; the important contribution of a barium meal examination to the diagnosis of primary incompetence would be the demonstration of reflux. Unfortunately, there is general agreement that the maneuvers designed by radiologists to demonstrate reflux are unreliable in any particular case.[1,3,13,17,18] Such tests for reflux are often negative when nonradiologic tests demonstrate significant reflux. Moreover, if a vigorous effort is made to induce reflux or the water swallowing or siphonage test is used, positive tests may be observed in patients who are, for all practical purposes, asymptomatic.[5,15,25] Operative intervention designed to create an antireflux mechanism may be recommended despite a completely negative barium meal examination or as a result of the demonstration of reflux of questionable significance. In one operative series, it was stated that "the most impressive feature of the X-ray studies is the thickness of the envelope containing the 'negative' barium films."[11]

In patients with heartburn, in order to prove the existence of competence of the lower esophageal sphincter, it is necessary to separate those with a sliding hernia from those without a hernia. The criteria used for placing patients in these 2 groups are therefore critical to the interpretation of the results. In one such study,[4] the cri-

* From the Department of Radiology, The Mount Sinai Hospital and the Mount Sinai School of Medicine of The City University of New York, New York, New York.

terion "of an easily demonstrable hiatus hernia, at least 3.0 to 4.0 cm. in diameter" was used. It is clear, however, that many hernias are smaller than this and require special radiologic attention in order to be identified. It has been pointed out that, in the study of 71 patients operated upon because of "incompetency of the gastric cardia without radiologic evidence of hiatal hernia,"[11] a correct roentgenologic diagnosis was possible in slightly more than a third, apparently because of the demonstration of a "patulous cardia" with marked reflux into the esophagus.

It is the purpose of this paper to emphasize that the roentgen appearance variously designated as a patulous cardia, chalasia, widening of the hiatus, malformation of the cardia and fundus of the stomach (malposition cardio-tubérositaire) is, in truth, evidence of a sliding hiatal hernia and is not purely functional in origin. Moreover, the important point is that this type of hernia is the type most likely to be the cause of reflux and heartburn. In order to demonstrate this, it is necessary to revise the conventional definition of a sliding hernia and to correct misconceptions about the anatomy of this area which have persisted despite well documented evidence to the contrary.

CONVENTIONAL DEFINITION OF SLIDING HIATAL HERNIA

The usual definition of a sliding hiatal hernia is that a portion of the stomach protrudes through the esophageal hiatus into the mediastinum (Fig. 1*A*).[10,20] This definition assumes that there is some well-defined, generally agreed upon, landmark to indicate the end of the esophagus and the beginning of the stomach,[20] and that this landmark coincides with the level of the hiatus. Landmarks which have been used by various authors, depending upon their points of view, include: (1) the sharply demarcated, but often zig-zag squamocolumnar mucosal junction or ora serrata or Z line; (2) the junction of the tube and the sac; (3) the level of the constrictor cardiae or sling fibers; (4) the level of the peritoneal reflection; (5) the distal extent of the peristaltic stripping wave; (6) the level at which Meissner's plexus appears; (7) a change in the appearance and direction of the arteries and veins or of the muscle fibers; (8) the lower limit of the esophageal submucosal mucous glands. These landmarks do not coincide with each other and do not identify the level of the hiatus. The most important discrepancy is the fact that the tube-sac junction or the cardiac orifice is located about 2.0 cm. below the hiatus (Fig. 1*B*). In other words, there is present normally a tubular channel continuous with the esophagus above the diaphragm which extends through the hiatus and into the abdomen before joining the saccular stomach at the cardiac orifice. As elevation occurs with herniation, this tubular segment would precede any "sac" of stomach (Fig. 1*C*). Radiologists have long been aware of this segment (Fig. 2, *A* and *B*).[22,27,28] In the roentgen literature,[28] this channel has been referred to as the "submerged segment," since it lies within the intraabdominal compartment and collapses during the course of a deep inspiration ("empty segment"). Unfortunately, anatomists have often denied the existence of this segment or rather the existence of an "abdominal esophagus" or claim that it is less than 1 cm. in length. The reason for this discrepancy is not difficult to discover. The column of barium visualized by the radiologist outlines the lumen of this segment and includes the thickness of the wall of the stomach at its distal end and the thickness of the crural fibers at its upper end. When the abdominal segment is exposed by the anatomist or the surgeon from the outside, these 2 portions are not evident and the visible part may appear insignificant. The existence of an abdominal tubular segment is also well documented by manometric studies which demonstrate that the distal 2 cm. or more of the lower esophageal sphincter lie within the abdomen between the hiatus and the cardiac

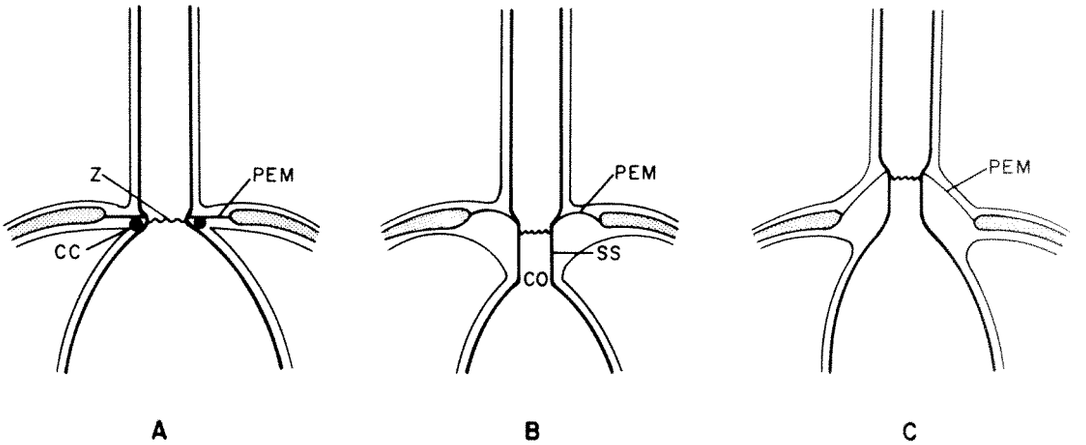


Fig. 1. Diagrammatic representation of anatomic relationships in the region of the hiatus. (*A*) Original concept on which the conventional definition of a sliding hernia was based. The tube-sac junction, the squamocolumnar mucosal junction (Z), the constrictor cardiae (CC) and the peritoneal reflection as well as the attachment of the phrenicoesophageal membrane (PEM) are all shown at the same level and at the level of the hiatus. If this were the true anatomy, any of these landmarks could be used and the earliest stage of herniation would be a portion of the saccular stomach or fundus dislocated above the level of the hiatus. (*B*) Current concept of the normal anatomy. There is a short tubular segment which extends from the upper aspect of the hiatus to the cardiac orifice (CO). The squamocolumnar mucosal junction may be anywhere from 1.0 to 3.0 cm. above the cardiac orifice. This intraabdominal segment has been referred to in the radiologic literature as the "submerged segment." The phrenicoesophageal membrane (PEM) is shown as having its main insertion a short distance above the mucosal junction. (*C*) Oversimplified representation of the first stage of herniation and elevation of the esophagogastric region. At this stage, no portion of the original saccular stomach extends above the level of the hiatus. The "herniated" portion is the original submerged segment. The phrenicoesophageal membrane (PEM) is stretched.

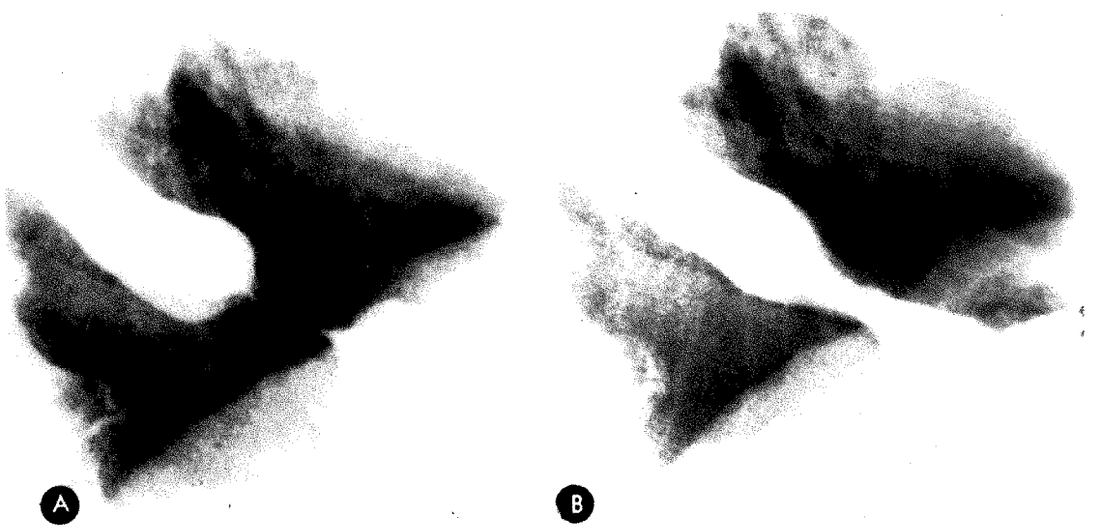


Fig. 2. (*A* and *B*) Successive 70 mm. spot roentgenograms show transient delay to the passage of fluid barium and an empty segment 2.0 or 3.0 cm. in length between the point of delay and the fundus of the stomach. The second frame shows barium traversing the previously empty segment, but it remains as a relatively narrow tubular channel. The upper margin of this segment is at the level of the entrance to the hiatus. The dome of the diaphragm is in a different plane and is an unreliable indication of the hiatal level. The hiatus itself cannot be identified.

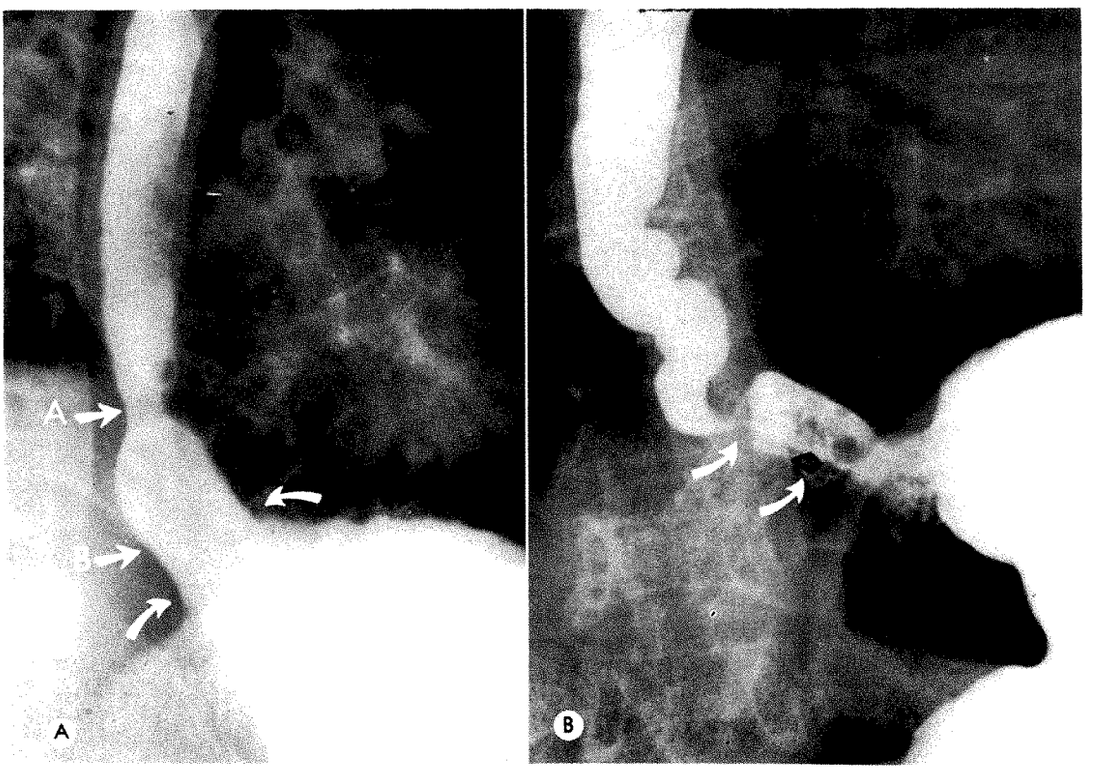


FIG. 3. (*A*) Roentgenogram taken prior to esophagoscopy shows a bell-shaped configuration between a functional ring (arrow A) and the fundus of the stomach. The width of the barium column (unlabeled arrows) traversing the hiatus is obviously widened and funnels distally to a patulous opening with the fundus. There is no ring to identify the mucosal junction but it is likely to be within the bell configuration (arrow B). (*B*) At esophagoscopy, a metallic clip was placed on the mucosal junction. A roentgenogram taken several hours later shows this clip (lower arrow, touched-up) mid-way between the hiatus and the functional ring (upper arrow). The original submerged segment has been displaced upward, but cannot be separately identified.

orifice. For practical purposes, therefore, the "submerged segment" seen by the radiologist and the site of the lower esophageal sphincter coincide. A surprising feature of the submerged segment, that is still not generally appreciated, is that it is lined in most of its extent by columnar epithelium continuous with and comparable to the cardiac epithelium of the saccular stomach (Fig. 1*B*). In other words, the squamocolumnar junction or the "Z" line is located within this segment and often at its upper end, that is, at the level of the hiatus.[14] Although attempts have been made to coin a special name for this abdominal segment, such as abdominal gullet, "cardia," cardiac antrum, and its lining epithelium has been referred to as "transitional epithelium,"[2,10] such names are not likely to be generally accepted and the designation "abdominal esophagus" probably will persist. The semantic problem becomes even greater in the presence of a sliding hernia since, when dislocated into the mediastinum, the distensibility of the "abdominal esophagus" increases and its tubular configuration is lost (Fig. 3, *A* and *B*). It is indeed strange that, when normally located below the hiatus, the "submerged segment" resembles the esophagus while, when displaced above the hiatus, it resembles stomach. In fact, when a large sliding hernia is present, the original submerged segment is incorporated into the

hernial sac. Offhand, it seems picayune to argue about the nature and existence of such a short tubular channel within the abdomen until one realizes that the essential function of the esophagogastric region, that is, the prevention of reflux, is based on the presence and integrity of this segment.

From the manometric point of view, under normal circumstances, the distal end of the high pressure zone identifies the cardiac orifice, and the point of respiratory reversal or point of inversion of pressure with respiration identifies the level of the hiatus. These 2 points are separated from each other by a distance of at least 2.0 cm. It would, therefore, seem straightforward, by comparing the distance between these 2 points, to identify minimal upward displacement of the submerged segment. However, this turns out not to be true. The point of respiratory reversal is dependent primarily on the gradient of pressure in the high pressure zone and ordinarily appears at the point of peak pressure which, normally, happens to be at the level of the hiatus.[9] Elevation of the sphincteric region therefore is not detectable if the sphincter is intact unless the distance to the nostrils or incisor teeth is obviously decreased. If the sphincter is incompetent, the point of respiratory reversal is usually difficult to identify and is often high up in the body of the esophagus. The identification of minimal elevation of the esophagogastric junction therefore depends on roentgenologic or esophagoscopic observations.

SUGGESTED REDEFINITION

Since the conventional definition of a sliding hernia is unsatisfactory, at least in regard to the problem of the identification of minimal herniation, some other definition is required. A single landmark such as the esophagogastric mucosal junction might be adopted by general agreement but the Z-line may normally be from 1 to 3 cm. above the cardiac orifice.[11] A more fundamental objection to this, however, is the fact that the specific location of the mucosal junction is irrelevant to the functional aspects of this region.[20] It should be possible to agree that the most basic feature of a sliding hiatal hernia of the acquired type—and therefore the best basis for its definition—is "stretching of the fascial attachments of the esophagogastric region to the diaphragm." The fascial attachments are generally referred to as the fascia of Laimer or the "phrenicoesophageal membrane."[2,7] This membrane contains many thick elastic fibers and extends from the margin of the crura of the diaphragm to—and into—the esophagogastric region. Under normal circumstances, this membrane is a definite, easily identifiable structure, although details as to its precise anatomy and role may be controversial.[6,10] It maintains fixation of the esophagogastric region to the diaphragm and closes the potential space between the esophagus and the diaphragm. Obviously, some loss of elasticity (increase in compliance) of this membrane is required to permit upward dislocation and herniation in the conventional sense (Fig. 4, *A* and *B*). This definition is of functional as well as etiologic and anatomic significance, since an intact phrenicoesophageal membrane is essential to the maintenance of a normal antireflux mechanism (Fig. 5).[7,16] Moreover, the phrenicoesophageal membrane plays the most important role in maintaining the normal configuration of the submerged segment since, during swallowing, the sphincter reflexly relaxes. Whenever a bolus passes through the submerged segment, additional volume must be created in the region surrounding this segment in order to make available the space required to accept the bolus (Fig. 6, *A* and *B*). The surrounding region is a relatively closed space bounded above by the phrenicoesophageal membrane and below by the peritoneal attachments with their subjacent viscera. The volume required to permit opening and filling of the submerged segment is created by the oncoming bolus which forces the phrenicoesophageal membrane upward, displacing some air from the adjacent bases of the lungs. The energy

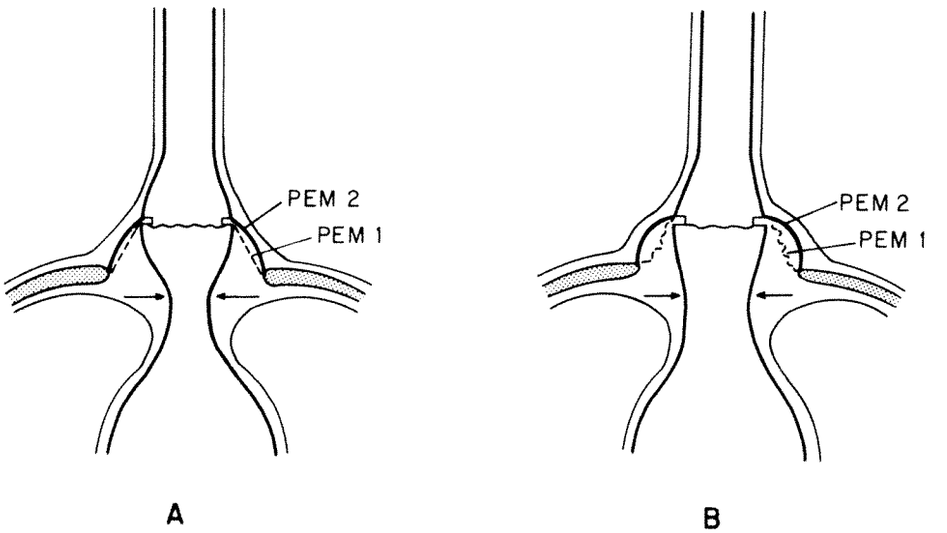


FIG. 4. Diagrammatic representation of minimal herniation and elevation of the esophagogastric region. (*A*) The position of the phrenicoesophageal membrane during filling (PEM 2) is not greatly different from its position in the resting phase (dashed line, PEM 1) because the slack of the stretched membrane was taken up before swallowing by shortening of the body of the esophagus. As a result, the width of barium column (unlabeled arrows) traversing the hiatus and entering the fundus of the stomach is relatively narrow. Pseudo-sphincteric activity will be evident at this site. (*B*) In this case, elevation of the esophagogastric region has not been sufficient to take up the slack in the stretched phrenicoesophageal membrane in the resting phase (PEM 1). As a result, the oncoming bolus has no difficulty in stretching the membrane (PEM 2) and the barium column in the region of the hiatus (unlabeled arrows) is easily distended and appears wide. Symptoms due to reflux are likely but their severity cannot be predicted.



FIG. 5. Postoperative cine frame of a dog after incision of the phrenicoesophageal membrane. Every effort was made not to damage the muscle of the esophagus or stomach. Barium in the fundus of the stomach passed freely into the esophagus on inspiration and back into the stomach on expiration. No obvious sac of stomach is present above the diaphragm, but the barium column in the hiatus is wide and joins the fundus of the stomach through a patulous opening.

imparted to the bolus by pharyngeal action or esophageal peristalsis must be sufficient to accomplish this. The fat within the closed space permits readjustment of the shape of the space as its configuration changes. The relatively limited distensibility of the submerged segment seen normally is therefore based on maintenance of intact elastic characteristics of the phrenicoesophageal membrane. Moreover, during emptying, as the bolus is propelled into the stomach, the elastic recoil of the phrenicoesophageal membrane plays a significant role in producing prompt collapse of the submerged segment and maintaining its

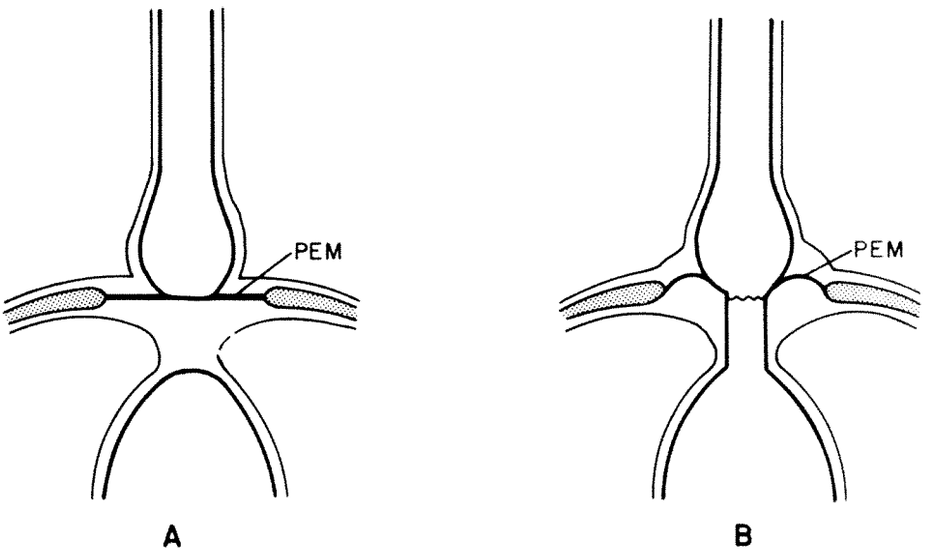


FIG. 6. Diagrammatic representation of the role of the phrenicoesophageal membrane in limiting distensibility of the normal submerged segment. (*A*) There is often delay in the passage of a fluid bolus at the hiatus while intraluminal pressure is built up in the body of the esophagus, despite the fact that the intrinsic sphincter begins to relax at the onset of a swallow. The phrenicoesophageal membrane (PEM) is shown as extending straight across the hiatus. (*B*) In contrast to a dry swallow, the oncoming bolus of fluid must have sufficient energy to distend the submerged segment before passage into the stomach can occur. Since the space between the peritoneal reflections and the phrenicoesophageal membrane (PEM) is essentially a closed space, the additional volume required to permit filling of the submerged segment must be created by stretching the phrenicoesophageal membrane upward and displacing some air from the bases of the lungs. The fat surrounding the submerged segment permits readjustment of the configuration of the space as its volume increases.

closed state. As the membrane loses elasticity, contraction of the longitudinal muscle of the body of the esophagus may produce shortening of the esophagus and elevation of the esophagogastric region, that is, a sliding hernia in the conventional sense. However, the degree to which such active shortening occurs or whether it will occur at all is unpredictable. The degree of shortening will, however, determine the resting length and tension in the phrenicoesophageal membrane and the degree to which further stretching can occur when a bolus traverses the region (Fig. 4, *A* and *B*). If almost all of the slack of the compromised phrenicoesophageal membrane is taken up by shortening of the esophagus, only a relatively small volume can be created by further stretching of the membrane; distensibility will be limited by this external constraint and the column of barium traversing the region of the hiatus will be relatively narrow. On the other hand, if considerable slack still remains in the resting state, the segment within the hiatus can easily be distended to a wide caliber and the elastic recoil during emptying is diminished. An unanticipated phenomenon occurs whenever the segment within the region of the hiatus, no matter what its nature, cannot distend to the same degree as adjacent segments. Any such segment will be the first to collapse as intraluminal pressure is decreased and opening of such a segment will require greater pressure.[29] Such relatively narrow segments show greater critical opening and greater critical closing pressures than their neighbors. As a result, any factor, intrinsic or extrinsic, which limits distensibility will produce pseudo-sphincteric action. On the other hand, if distensibility is excessive and con-

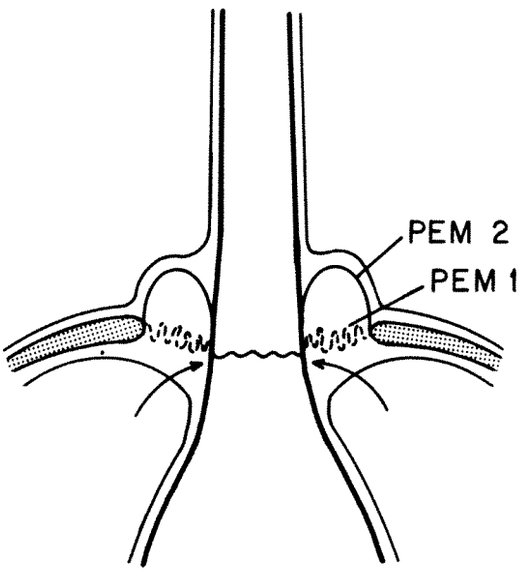


FIG. 7. Diagrammatic representation of herniation with *no* elevation of the esophagogastric region—*no* stomach above the hiatus. Despite loss of elasticity and stretching of the phrenicoesophageal membrane, the esophagus has not shortened in the resting phase or during the course of a swallow. The lax membrane in the resting phase (dashed line, PEM 1) is easily displaced upward (PEM 2) creating little resistance to filling and permitting excessive distention of the submerged segment (between arrows). A wide continuous column of barium traverses the hiatus and opens into the stomach through a patulous cardiac orifice. The level of the mucosal junction is indicated but is not evident roentgenologically.

tractility or elastic recovery decreased, free and easy flow through the relatively wider segment can be anticipated.

The description of the interplay between stretching of the phrenicoesophageal membrane and shortening of the esophagus serves to explain why, with the same degree of upward displacement, some patients will show reflux through the hiatal region while others will not. It is also possible, however, to conceive of the situation in which the phrenicoesophageal membrane is stretched, but there is no significant shortening of the esophagus in the resting state or during the course of a swallow (Fig. 7). Since the slack of the phrenicoesophageal membrane is not taken up at all, the membrane remains lax and no great force or pressure is required to fill and distend the submerged segment. Roentgenologically, there would then be evidence of an unusually wide column of barium traversing the region of the hiatus and a patulous communication with the stomach. Stretching of the phrenicoesophageal membrane, that is, a hernia in accordance with the suggested redefinition, can be diagnosed despite the fact that the submerged segment may be normally located. Radiologically, the resulting configuration will be difficult to distinguish from that illustrated in Figure 4*B* if a mucosal ring is not evident. The significant point is that this distinction is of no great importance—symptoms due to reflux are likely to be present in both instances (Fig. 8, *A–D*). Both have hernias and both are treated, medically and surgically, in the same fashion. From a practical point of view, the redefinition suggested, therefore, turns out to be very useful since, whenever a wide barium column traverses the region of the

FIG. 8. Four examples of hiatal herniation without any obvious sac of stomach above the hiatus—"chalasic" type of sliding hiatal hernia. (*A*) A newborn with free reflux in the inverted position shows marked widening of the "submerged segment." It is likely that this segment as well as the phrenicoesophageal membrane failed to develop normally during fetal life. Such children usually develop a normal submerged segment and lower esophageal sphincter in a period of months. (*B*) An adult showing free reflux (arrow) in Trendelenburg position. No normal submerged segment is evident and it probably has been displaced upward above the hiatus. (*C*) Another adult showing effacement or absence of the submerged segment. (*D*) Another adult with a similar appearance. Thick vertical folds can be faintly seen within the barium column traversing the hiatus, but cannot be identified as either esophageal or gastric. Folds such as these show no discontinuity at the mucosal junction.

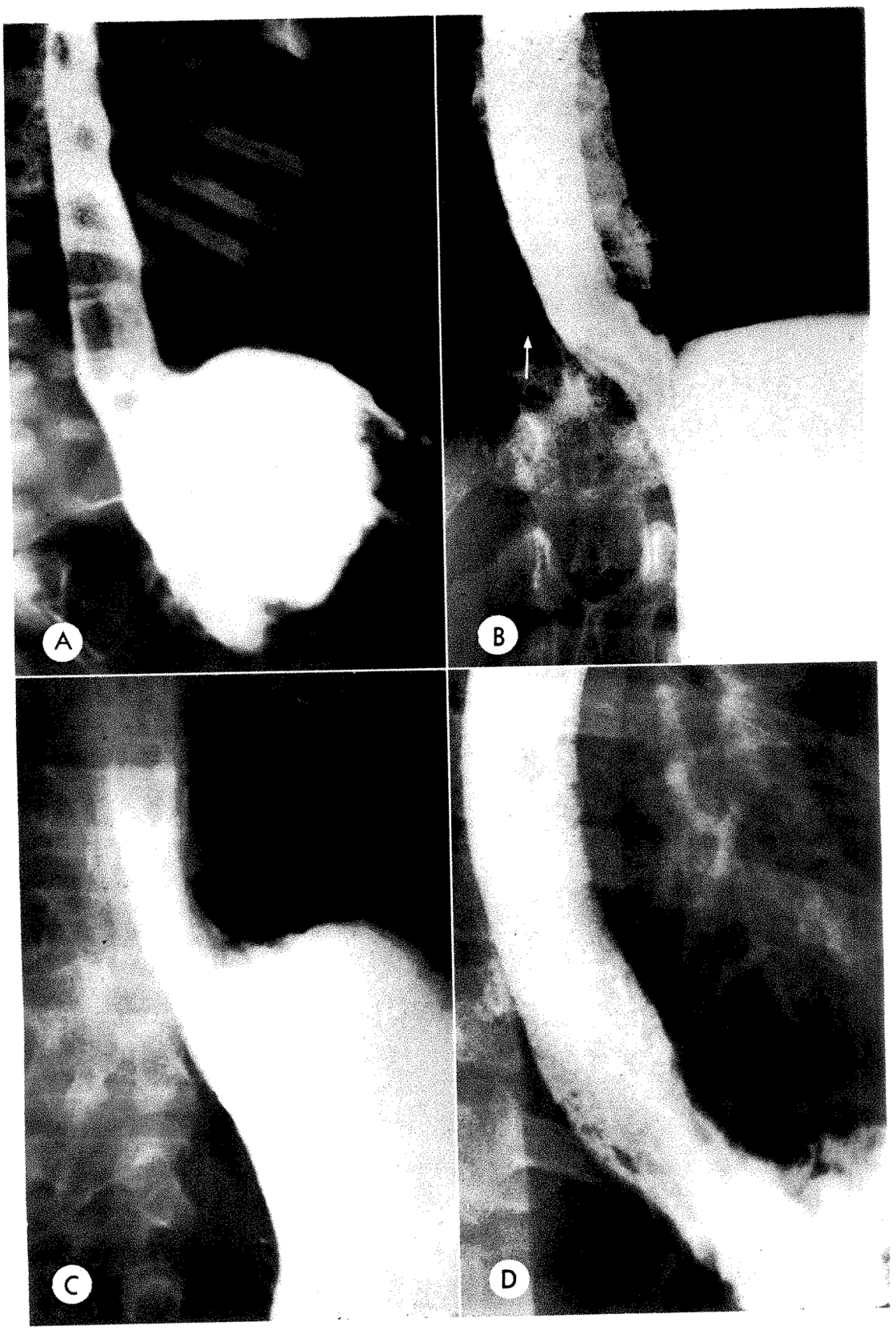

A
B
C
D



FIG. 9. Two cases demonstrating that the diagnosis of hiatal herniation can be made without specifically identifying the level of the hiatus. (*A*) This patient with periodic dysphagia and heartburn shows a fairly well-marked Schatzki ring. A hiatal indentation or significant pinchcock action could not be demonstrated.

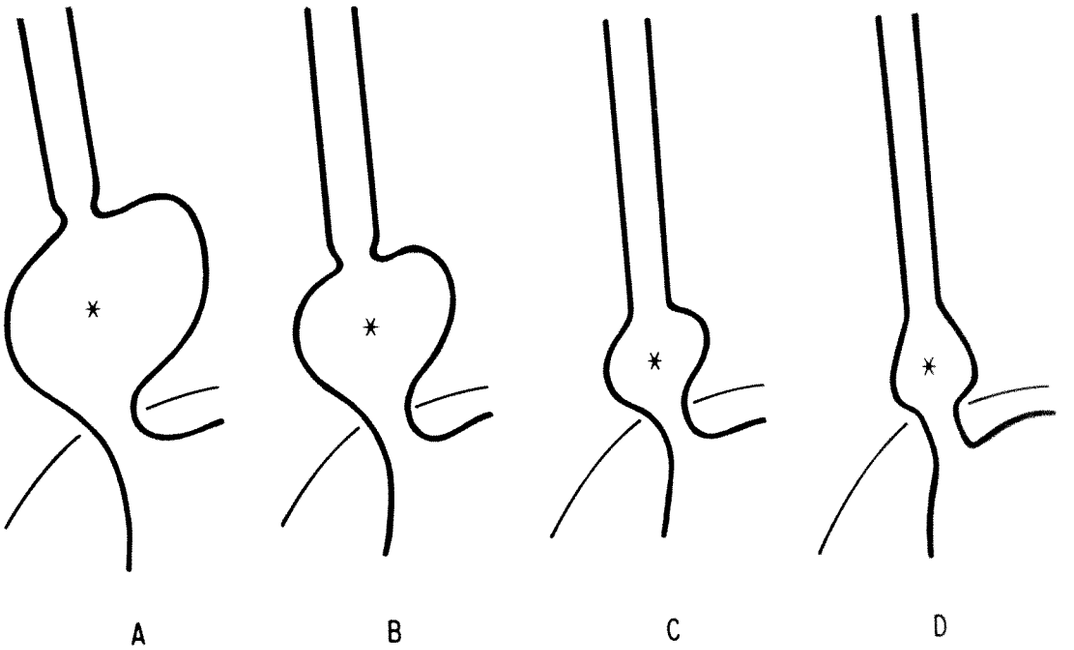


Fig. 10. (*A–D*) Diagrams illustrating the difficulty in identifying a "sac" of stomach above the diaphragm. Hiatal hernias (asterisks) of diminishing size from *A* to *D*. In the earliest stages, *C* and *D*, it may be impossible to distinguish a normal phrenic ampulla from a herniated portion of stomach or a sac composed of elements of both. This distinction is of little or no clinical significance if—as shown in this illustration—the barium column traversing the hiatus is narrow.

hiatus, one can assume that the phrenicoesophageal membrane is stretched, that a hernia is present, and that symptoms are likely—with little concern about the exact levels of the esophagogastric junction or of the hiatus (Fig. 9, *A–C*). To avoid argument as to whether or not a portion of the stomach is above the hiatus, this type of hernia may be referred to as the "chalasic" type of hiatal hernia. The definition of minimal herniation after hernia repair is also a difficult semantic problem, but a wide barium column postoperatively is nevertheless indicative of a poor result. "Widening of the hiatus alone" is a sign and the most significant sign of a potentially symptomatic hiatal hernia (Fig. 10, *A–D*; and 11, *A–D*). No other roentgen feature is required to make this diagnosis. Heroic efforts and repeated or prolonged examinations to demonstrate a hernial sac or "stomach" above the diaphragm are unnecessary. A maneuver such as the Valsalva procedure may actually be self-defeating by producing an artificial decrease in the width of the barium column in the hiatus. Placing a bolster underneath the abdomen of the patient may succeed in displacing a portion of the stomach into the mediastinum and convince the skeptical that a hernia is really present. The redefinition incidentally makes it unnec-

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It might be argued that this was a rare example of a mucosal ring without a hernia. However, the obviously wide barium column joining the esophagus to the fundus of the stomach is sufficient to warrant the diagnosis of a sliding hernia. (*B* and *C*) In this patient with heartburn, there was an elongated dilatation between the esophagus and the fundus of the stomach with a patulous communication. It is likely that the distal portion of this elongated "ampulla" is the result of herniation, but the presence of a hernia need not be debated, since the barium column traversing the region of the hiatus is obviously widened.

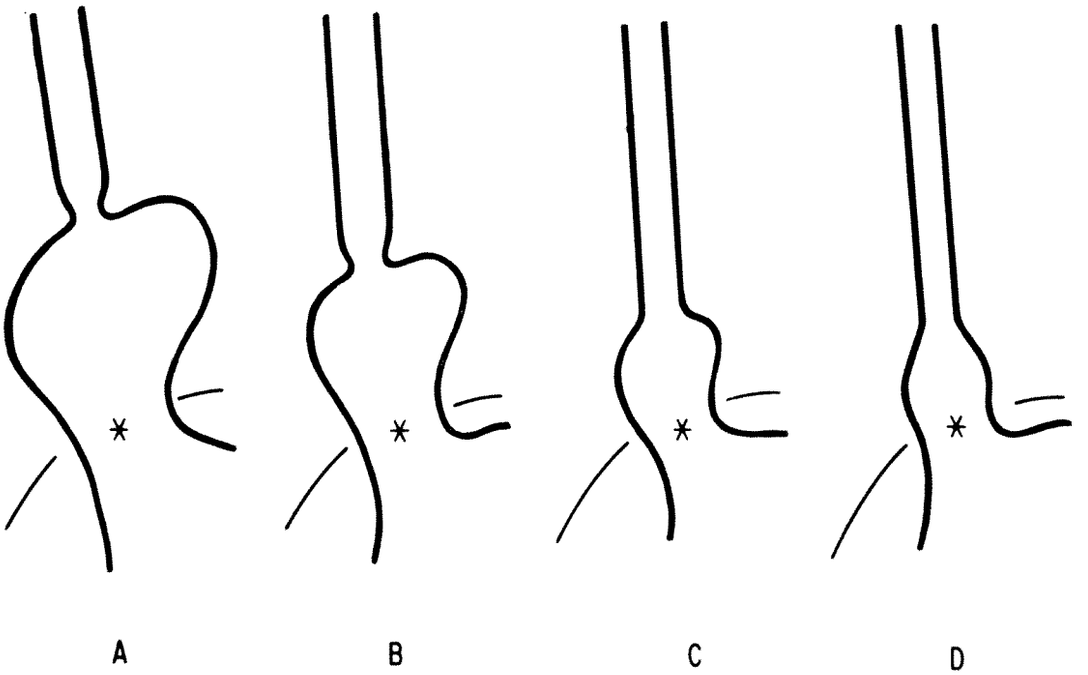


FIG. 11. (*A–D*) Similar configurations as in Figure 10, *A–D*, but the region of the hiatus (asterisks) is wide in each case. These are all hernias despite the fact that in *C* and *D* no significant portion of stomach may be elevated above the hiatus.

essary to speak of a "predisposition to herniation" without a bolster and a hernia with the bolster in the same patient at the same time. The bolster maneuver may not, however, give a correct picture of the potential width of the barium column traversing the hiatus, since the portion of the stomach trapped within the hiatus under these circumstances is often narrow and nondistensible. In fact, such displacement often seems to be one mechanism by which free reflux can be prevented.

Admittedly, it is not easy to judge the normal limits for the width and length of the submerged segment. It certainly cannot be done from a single random roentgenogram, but must be determined during the course of fluoroscopic observations. The width and configuration of the barium column traversing the hiatus are ordinarily best evaluated in the conventional prone position with the left side elevated as the patient drinks fluid barium rapidly. The observer must, however, use the technique that he is thoroughly familiar with and be certain that the patient is not retching or belching. The first swallow of barium in the erect position—a very familiar view—may be highly suggestive (Fig. 12, *A* and *B*). Marked variations in the appearance of the barium column in the region of the hiatus occur depending on the force generated by the pharynx and esophagus during any particular phase of swallowing. If peristaltic activity is poor or a proximal stricture present, it may not be possible to evaluate this area. In a general way, the normal submerged segment should be at least 2.0 cm. in length and no more than about 2.0 cm. in width. Precise figures, however, are not too meaningful since there is ordinarily also a change in configuration of the esophagogastric region with funneling of the uppermost portion of the stomach as it extends to and through the hiatus. Debatable changes in the appearance of the submerged segment are rarely of significance. It must, however, be

emphasized that, more often than not, the width of the barium column in the region of the hiatus in patients with small hernias is not uniformly increased. "Widening of the hiatus" occurs usually predominantly in the long axis of the hiatus, that is, backward and to the right. As a result, in the usual right anterior oblique position, the over-all diameter of the segment within the hiatus is increased, but individual folds are still apparent within the segment (Fig. 13, *A* and *B*). This indicates that, in a direction at right angles to the right anterior oblique projection, the segment is, in truth, narrow and compressed. Such a slit-like cuff of stomach within the hiatus also shows pseudo-sphincteric activity. A truly "patulous" channel must be uniformly circumferentially widened as indicated by a completely opaque barium column effectively obliterating the fold pattern during filling. If the barium column is widened only in one direction, a hernia is present but significant symptoms of reflux are unlikely.

The problem of the existence and the frequency of "primary incompetence" of the lower esophageal sphincter requires further investigation since many patients so classified in the past have had hiatal hernias.[11] When operated upon, some of these patients have shown portions of the stomach above the diaphragm or at least "laxity of the hiatal muscular sling."[11] The hypothesis described above as to the role of the phrenicoesophageal membrane in the antireflux mechanism does not explain all of the phenomena associated with this region. Nevertheless, experience indicates that a solidly filled, straight, wide barium column connecting the esophagus to the stomach which fills promptly is frequently associated with symptoms of reflux, even though barium reflux may be difficult to demonstrate. The relationship certainly is not quantitative and the severity of the

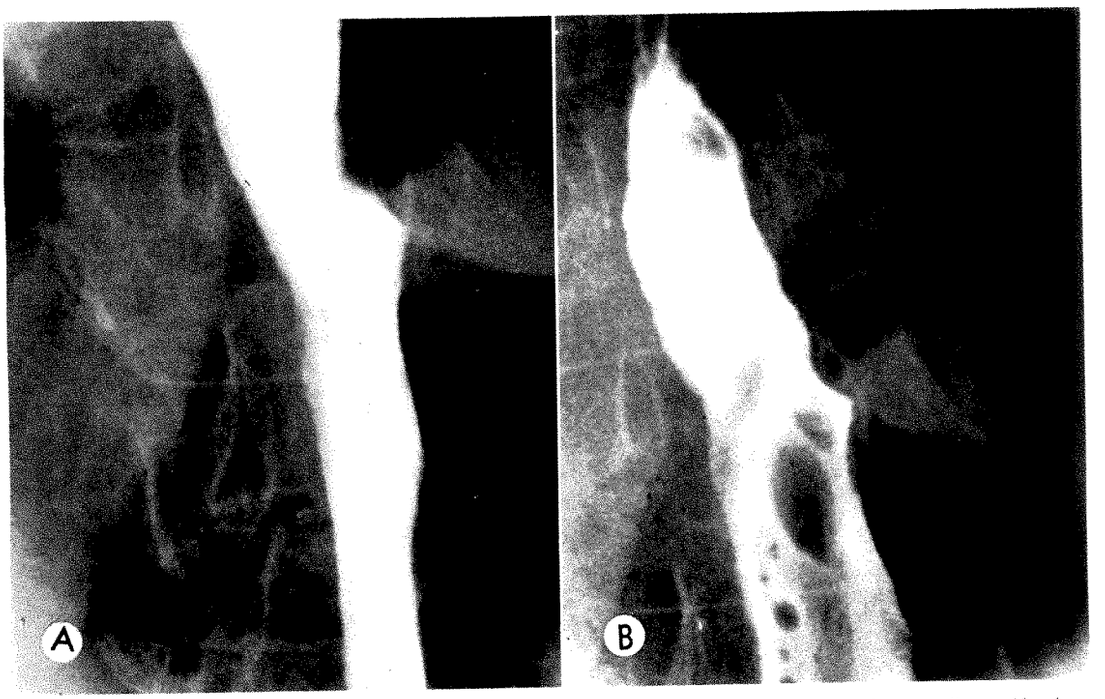


FIG. 12. (*A* and *B*) These 70 mm. spot roentgenograms taken during the course of the first swallow of barium in the erect position show widening or effacement of the submerged segment and immediately create the suspicion of a sliding hernia. This was confirmed by observation of a "sac" in the recumbent position.

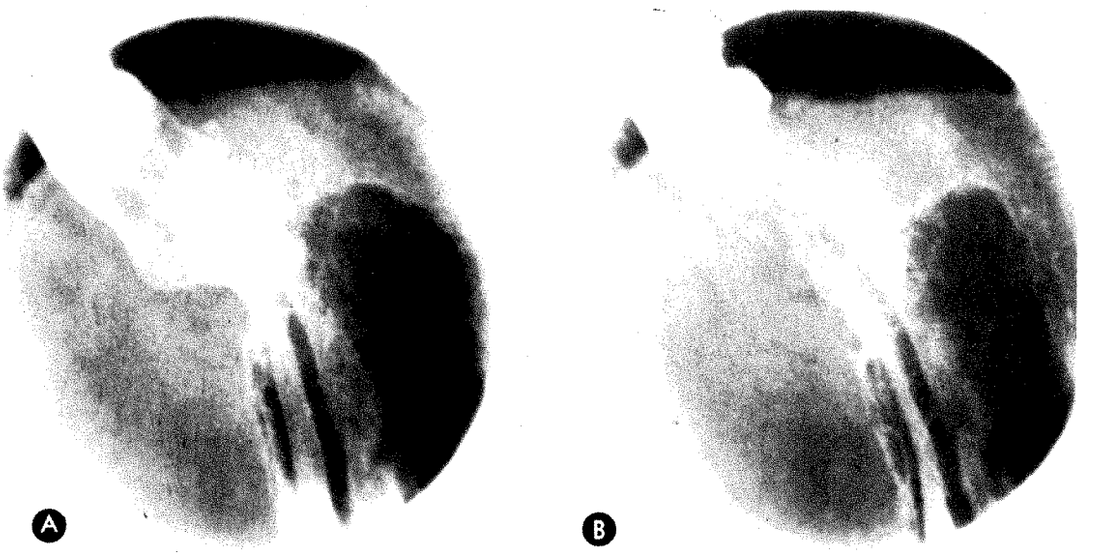


Fig. 13. (*A* and *B*) Patient with a slit-like cuff of the stomach within the hiatus; 70 mm. frames show persistent thick folds, probably rugae, in the region of the hiatus. The width of this segment is increased in this projection but must be much smaller in the opposite direction. Even a shallow inspiration (*B*) shows complete emptying of this segment.

symptoms cannot be predicted. It must be assumed that this appearance also denotes some degree of incompetence of the "intrinsic" component of the lower esophageal sphincter. The intrinsic component *per se* cannot be evaluated roentgenologically since the sphincter relaxes during swallowing of the barium. It is possible that the extrinsic mechanism provided by an intact phrenicoesophageal membrane may be adequate to prevent significant reflux in the absence of any intrinsic sphincteric activity. Such patients might appear quite normal roentgenologically and would not ordinarily come to manometric study because of the lack of symptoms. Their manometric characteristics are in truth unknown. This is in contrast to achalasia in which failure or incomplete relaxation of the sphincter manometrically is evident roentgenologically by persistent narrowing of the submerged segment. It is quite difficult by any method to separate intrinsic from extrinsic sphincteric or antireflux factors. In judging intrinsic sphincteric competence, it might seem, for example, that reflux after excessively forceful dilatation for achalasia (Fig. 14, *A–D*) would be the result of damage to the intrinsic sphincter, but it is likely that in such instances damage to the phrenicoesophageal membrane was also produced. An occasional case of scleroderma shows reflux without an evident hernia (Fig. 15), but biopsy of the phrenicoesophageal membrane in patients with scleroderma has demonstrated sclerodermatous involvement. This is not to deny that there may well be cases of reflux with severe heartburn and esophagitis due exclusively to incompetence of the intrinsic sphincter. It seems unlikely, however, that this occurs with anything like the frequency with which it has been reported. Certainly, heartburn can occur without a hernia by any definition and in some individuals, it is possible that "physiologic" reflux acting on a supersensitive esophageal mucosa may be the cause of severe symptoms. Such patients with purely functional heartburn should nevertheless be separated from those with an anatomic abnormality in

order that the effects of medical or surgical therapy can be reasonably evaluated.[17] Moreover, this type of functional reflux and heartburn may have metabolic, hormonal or psychogenic components or be the result of pathologic disturbances elsewhere in the abdomen such as cholecystitis. Operative intervention for a purely functional abnormality is likely to be much less successful than intervention performed for an anatomic defect.[7] Patients with the "chalasic" type of hiatal hernia should, however, not be excluded from the organic category. When no abnormality is seen on roentgen examination, the clinician must be wary of a truly functional abnormality, which may not be primary or confined to the lower esophageal sphincter (Fig. 16, *A–C*).

SUMMARY

The conventional definition of sliding hiatal hernia is revised and misconceptions about the anatomy of this area are discussed.

It is emphasized that the roentgen appearance variously designated as a patulous cardia, chalasia, widening of the hiatus,

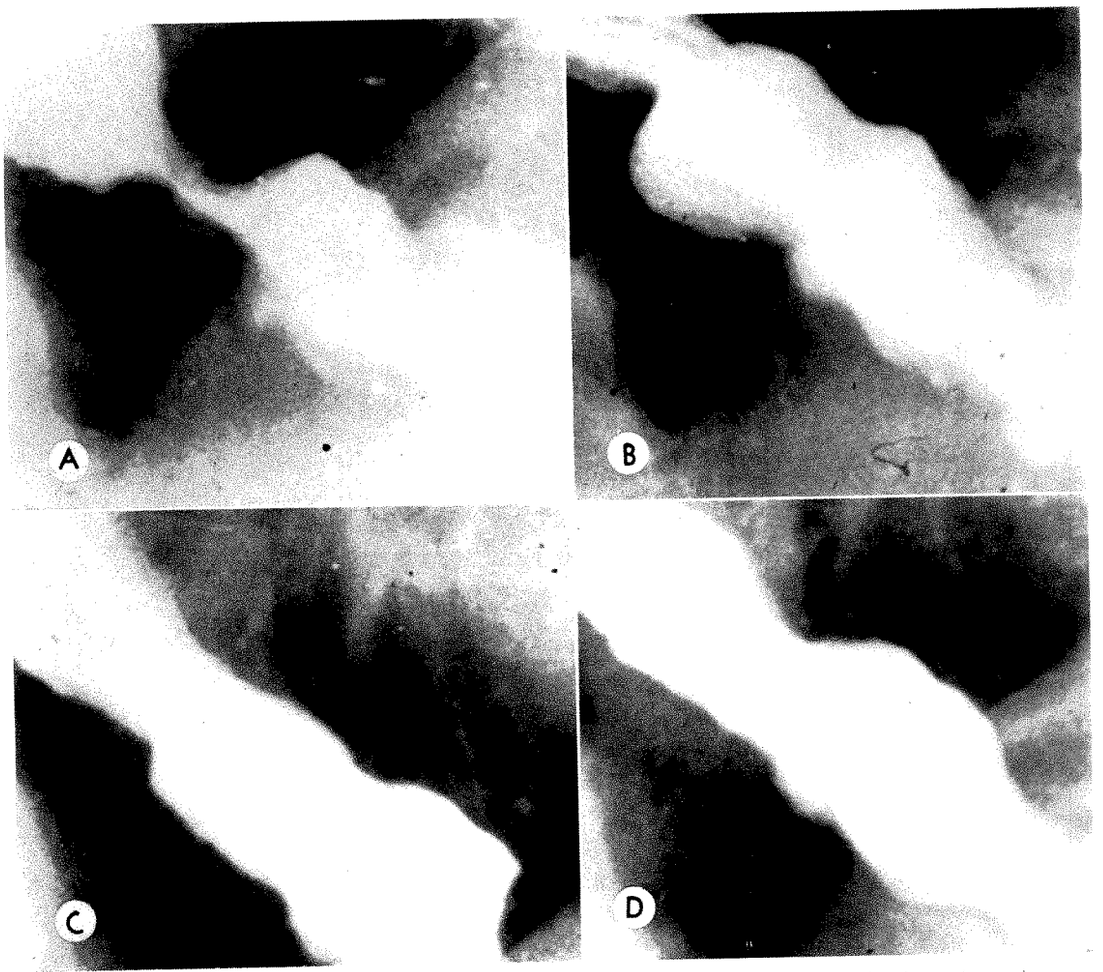


FIG. 14. (*A–D*) Patient with free reflux after forceful balloon dilatation for achalasia shows irregular contractility as well as a wide barium column traversing the hiatus. This may be an example of reflux due to tearing of the sphincter, but the possibility of damage to the phrenicoesophageal membrane as well cannot be excluded.



FIG. 15. Patient with scleroderma shows marked widening of the submerged segment which is normal in position. Reflux in such patients may be the result of sclerodermatous involvement of the intrinsic sphincter, but similar involvement of the phrenicoesophageal membrane has been demonstrated in other patients at operation.

malformation of the cardia and fundus of the stomach (malposition cardio-tubéro-sitaire) is, in fact, evidence of a sliding hiatal hernia and is not purely functional in origin.

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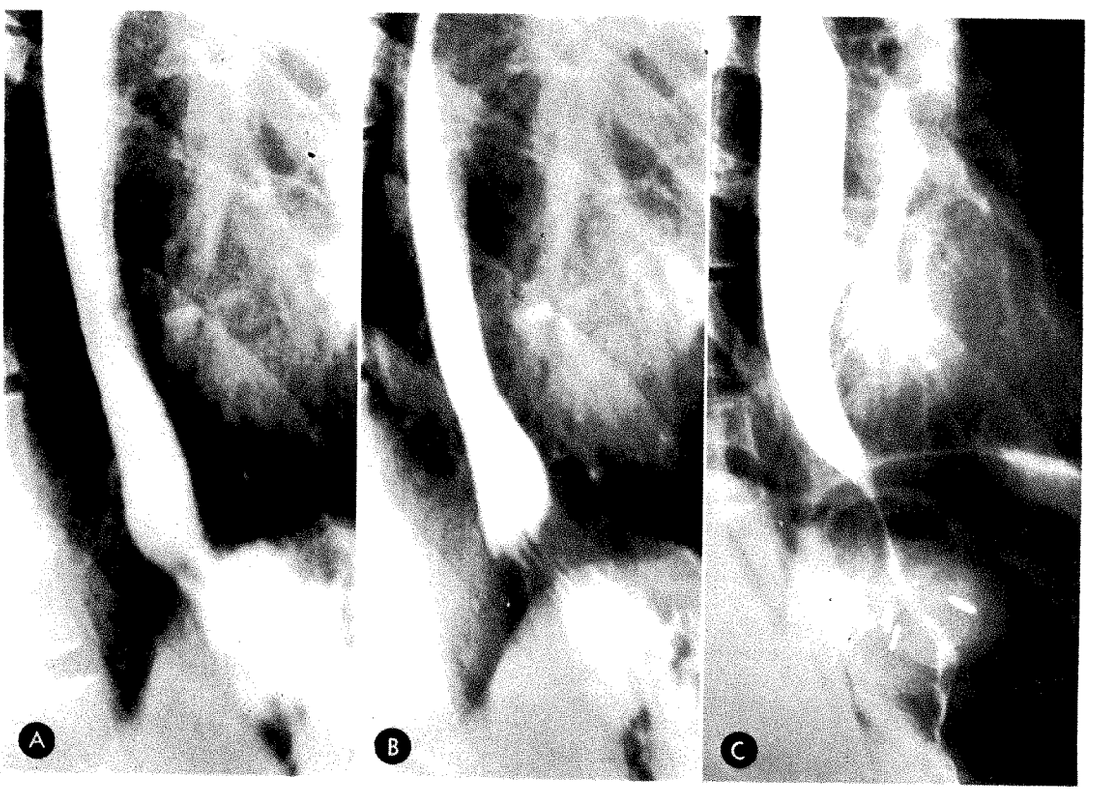


FIG. 16. A 30 year old female with severe heartburn, difficulty in swallowing and loss of weight. (*A* and *B*) No definite abnormality appeared to be present in the esophagogastric region. There was minimal decrease in distensibility in the mid-portion of the body of the esophagus and diminished peristaltic activity in this area on manometric examination. There was, however, no other evidence to suggest scleroderma. Because

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of severe symptoms, operation was recommended. (*C*) The appearance after a Belsey Mark IV type of repair shows a long narrow segment connecting the esophagus and the stomach. There is considerable air in the fundus of the stomach and a filling defect characteristic of this type of repair. There was only transient improvement in the patient's symptoms.

FORAMEN OF MORGAGNI HERNIA WITH VOLVULUS OF THE STOMACH*

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BETWEEN the costal and sternal attachments of the diaphragm on each side, a potential triangular space exists. Ever since Morgagni described it in his monograph in 1769, this space has been referred to as the foramen of Morgagni.[3,9] No muscle fibers are present in this area. Fat content is increased with obesity and may enlarge the space to the extent that a hernia is possible. Rapid changes in intra-abdominal pressure (trauma), and degenerative changes (aging) increase this possibility. Because of the pericardium, hernia is rare on the left, but may occur, even into the pericardium.[1,10] Occasionally, sternal attachments are absent, creating a large potential space, which may be associated with protrusion of the lower sternum.[2]

The symptoms are related to mechanical changes in the omentum, colon, stomach, small bowel, liver, or gallbladder. Most hernias contain omentum only and are asymptomatic. They may be distinguished on the lateral roentgenogram of the chest by the properitoneal fat around the herniated omentum.[7] Those hernias that contain transverse colon and omentum are usually asymptomatic, but when the stomach is involved, volvulus and torsion are likely. These complications are serious and produce rapid onset of high obstruction with retching, and, at times, inability to vomit. Significant morbidity and mortality attend, as patients are usually old and the correct diagnosis may not be established before gangrene and peritonitis have developed. The diagnosis depends upon the radiologist.

Although hernia through the foramen of Morgagni is considered rare, a fair number has been reported in the literature. A few of these have involved the stomach.[2,4–6,8,11,12] The following case reports describe 2 such hernias that were accompanied by volvulus of the stomach.

REPORT OF CASES

CASE I. An 84 year old white man was admitted acutely ill with epigastric burning, nausea, and retching of 8 hours' duration. A hernia through the foramen of Morgagni, which contained colon, had been documented by barium enema examination 10 years previously. Roentgenography revealed right foramen of Morgagni hernia that contained stomach and colon, and a gastric volvulus (Fig. 1; and 2, *A* and *B*). At surgery, the roentgen findings were confirmed.

CASE II. This 79 year old white man was admitted to the hospital with a history of vomit-

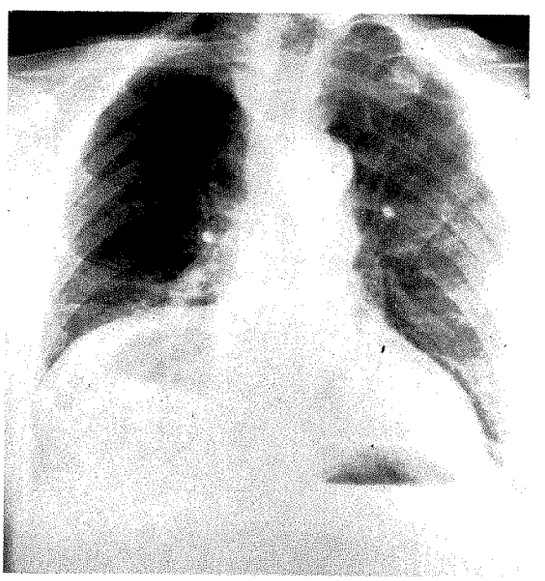


FIG. 1. Case I. Roentgenogram of the chest showing typical appearance of hernia through the foramen of Morgagni. In this view, the gas bubble on the right is in the inverted gastric antrum; that on the left is in the fundus.

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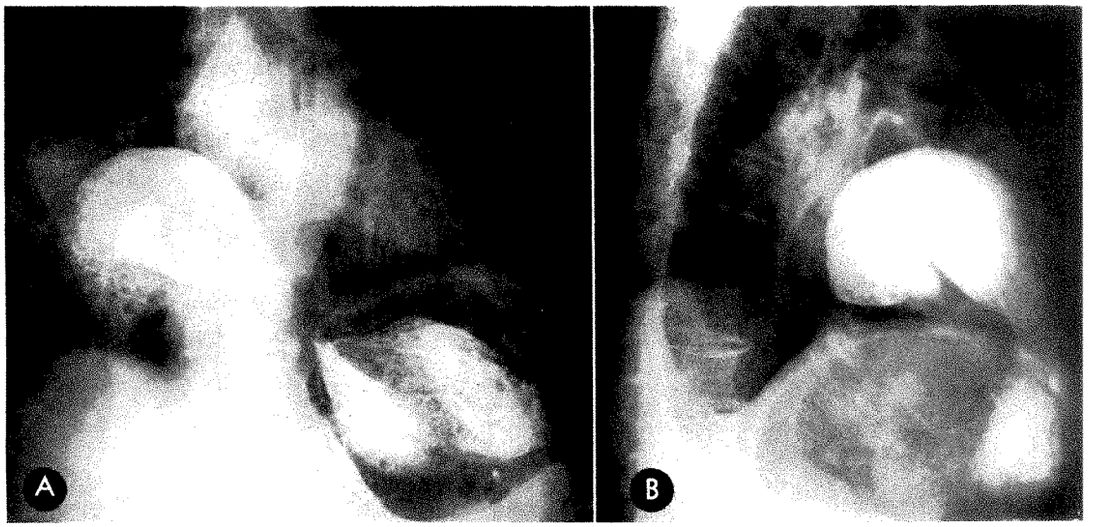


Fig. 2. Case I. (*A*) Typical appearance of herniation of the stomach through the right foramen of Morgagni with volvulus. The gas to the right of the inverted antrum is in the herniated transverse colon. (*B*) Lateral view showing the anterior position.

ing blood, and upper abdominal distention of several hours' duration. He had fallen 9 months previously. A hiatal hernia, umbilical hernia, and left inguinal hernia were known to be present.

Roentgenograms revealed a hernia through the right foramen of Morgagni, which contained colon, and volvulus of the stomach (Fig. 3, *A* and *B*; and 4). At operation the roentgenographic findings were confirmed.

DISCUSSION

As shown by the above cases, gastric volvulus may be present with or without

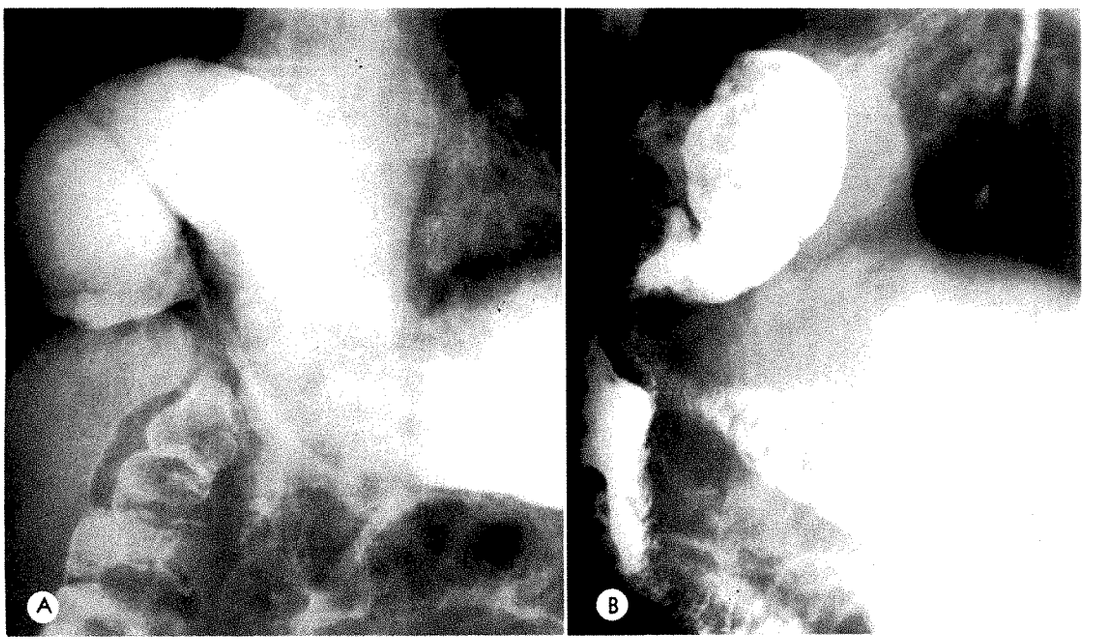


Fig. 3. Case II. (*A*) Herniation of the transverse colon through the right foramen of Morgagni. (*B*) Lateral view showing the anterior position.



FIG. 4. Case II. Volvulus of the stomach. The greater curvature of the antrum is rotated 180° on its long axis and is pulled up and to the right toward the mouth of the hernia by the gastrocolic ligament. Twists are seen in the body of the stomach and in the distal antrum.

herniation of the viscus. In Case II the stomach appears to have been rotated and pulled up and to the right by the gastrocolic ligament. Attachments between the colon and stomach may vary in length, and, in fact, with most herniations of the transverse colon through the foramen of Morgagni, the stomach remains in normal position. The hernia of Case I contained only colon for many years. Herniation of the stomach resulted in acute volvulus and obstruction.

Hernias through the foramen of Morgagni must be considered in the differential diagnosis of all lesions in the lower anterior chest (Fig. 1).

SUMMARY

Two cases of foramen of Morgagni hernia with volvulus of the stomach are reported.

In both instances the correct preoperative diagnosis was established by roentgenologic examination.

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DIFFUSE ESOPHAGEAL SPASM*

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SINCE the first description of esophageal spasm by Osgood,[13] scattered reports describing the clinical, manometric or roentgenographic features have appeared in the literature.[3,8,9,14,16] Ferguson *et al.*,[7] on the basis of manometric and cineroentgenographic studies, state that the process is a distinct functional disorder. Bennett and Hendrix[2] on the other hand, consider the syndrome secondary to multiple causes and question the existence of a separate clinical roentgenographic entity. The pathogenesis of esophageal spasm has never been clearly identified and documented; hence, the management of these patients is varied and not well defined.

The purpose of this communication is to document our experience with a group of 55 patients seen at the University of Kansas Medical Center during the last 5 years. A diagnosis of diffuse esophageal spasm had been made in all instances. Analysis of the roentgenographic findings has demonstrated that the patients could be grouped in rather specific categories. The roentgenographic categories have been correlated with manometric studies and various clinical findings. The importance of an accurate diagnosis is stressed. The management and prognosis of the different patient groups appear to be entirely related to the underlying cause of the changes in esophageal motility. The significance of the various diagnostic modalities with particular attention to the roentgenographic features is discussed. The possibility of both primary and secondary esophageal spasm will be presented.

MATERIAL AND METHOD

During the past 5 years a total of 55 patients have been evaluated by the Gastroenterology and Radiology Services. This evaluation included a complete history with emphasis on gastrointestinal tract symptomatology and pertinent laboratory studies. Intraluminal esophageal manometry was performed on 29 of the patients and roentgenographic evaluation was achieved in all of them. Of this original group, 24 patients did not fulfill the diagnostic criteria of esophageal spasm either by manometric or by roentgenographic studies. Therefore 31 patients form the basis for this report.

Manometric studies were performed by introducing a 4-lumen tube with 3 openings 5 cm. apart into the esophagus. The tube was filled with saline solution and connected to pressure transducers for recording. Spastic activity was defined as abnormal motor activity in which intraesophageal pressure was simultaneously elevated at 2 or more recording places (Fig. 1*B*). These abnormal contraction waves were found to be repetitive and therefore nonpropulsive.

Roentgenographic evaluation by means of fluoroscopy, spot roentgenography and cinefluoroscopy was carried out on 2 or more separate occasions on all patients. The patients were examined in the prone position with the left side elevated approximately 45°. Liquid barium was used and no attempt was made to increase intraabdominal pressure. Maximum distention of the esophagus was achieved by repeated swallows of barium. The diagnosis of diffuse esophageal spasm was made on the basis of the lack of progression of the primary esophageal wave (or stripping wave) distal to the aortic arch. The normal wave was replaced by simultaneous repetitive contractions occurring diffusely over the entire lower portion of the esophagus (Fig. 2). Associated findings were

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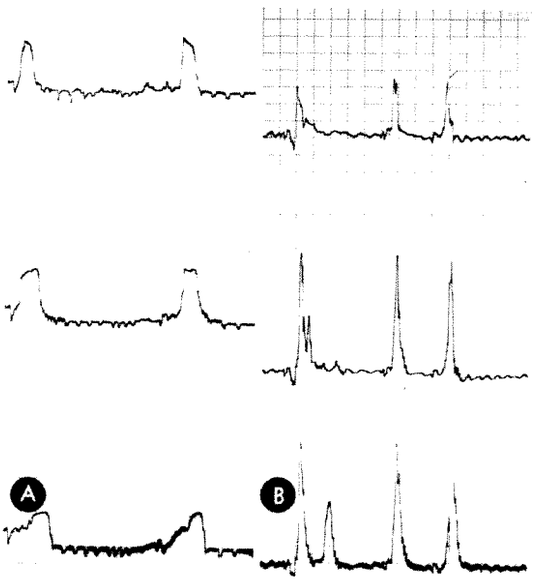


FIG. 1. Pressure recordings. (*A*) Normal motility pattern. Note the sequential progression of the stripping wave. (*B*) Esophageal spasm. The sequential pattern is lost. Simultaneous contractions are evident at all 3 leads. Note also the elevation of the peak pressure.

thickening of the lower esophageal wall and contraction of the esophageal lumen.[9]

RESULTS

The correlation of the manometric and roentgenographic findings clearly identified 4 categories of patients.

The first group of 7 patients (Table I) had manometric changes compatible with esophageal spasm, but completely normal roentgenographic findings. The manometric findings did not appear to be consistent except for 2 patients (H.L. and R.S.). The symptomatology in these patients was somewhat vague and of rather short duration and not very specific. Acid perfusion tests were performed in 3 patients; 2 of them were positive and 1 was negative.

A second group of 11 patients (Table II) had manometric evidence of spasm and varied roentgenographic changes which were not considered to be characteristic of spasm. Nine patients had a hiatal hernia and demonstrable gastroesophageal reflux. Six patients had motor dysfunction manifested by delayed emptying of the esophagus. These changes are known to be found in patients with esophagitis secondary to reflux.[12] The presence of a hiatus hernia with gastroesophageal reflux and various degrees of motor failure suggests that in the majority of these patients the symptomatology could be explained by esophageal reflux and associated esophagitis.

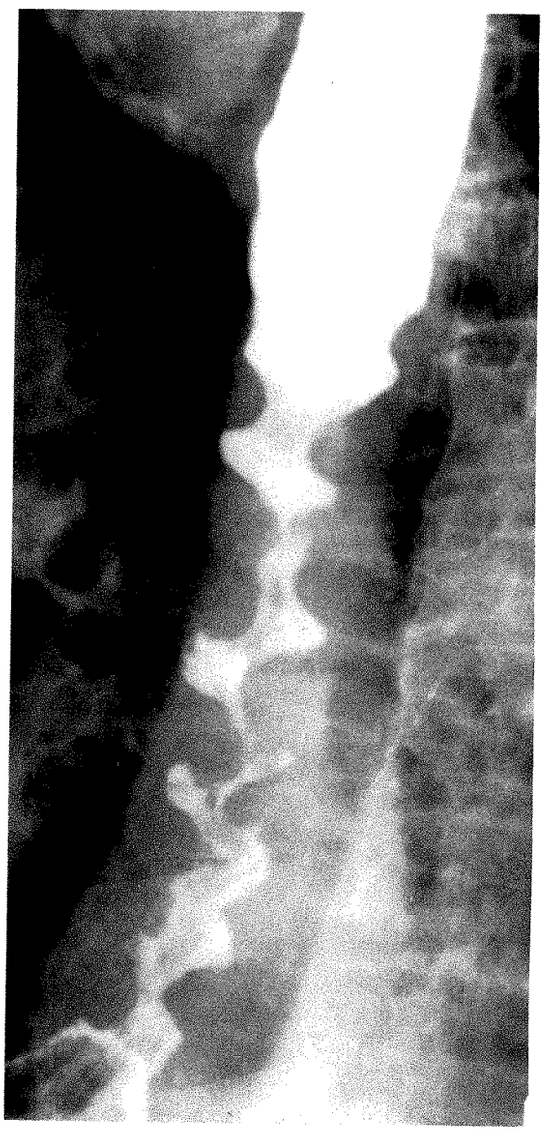


FIG. 2. Diffuse contractions of the lower esophagus are noted with formation of "pseudodiverticula"—"corkscrew" appearance.

TABLE I

FIRST GROUP OF PATIENTS

	Age	Sex	Symptomatology	Manometric Findings	Roentgenographic and Fluoroscopic Findings
H.R.	62	F	Intermittent dysphagia for solids; choking sensation; 5 months duration	Occasional high pressure spasm waves; Berstain test negative	Normal
J.H.	54	M	Intermittent dysphagia; "can't breathe while I am eating" liquids and solids; 1 year duration	Few spasm waves and nonpropulsive peristalsis noted in the body	Normal
S.J.	49	F	Epigastric and chest pain; 7 months duration	Repetitive contractions; abnormal peristalsis suggestive of spasm; Berstain test positive in paper, negative for pain	Normal
D.F.	18	M	Back pain relieved by belching, worse at night; some vomiting and dysphagia; hyperchloridia	Small amplitude spasm waves with poor propagation; Berstain test positive	Normal
C.F.	26	M	Heart burn; epigastric pain; nausea	Normal, but pain reproduced with Berstain test as well as production of abnormal waves suggestive of spasm	Normal
H.L.	28	F	Intermittent epigastric and chest pain, 1–2 times a month; 1½ years duration	Multiple instances of simultaneous contraction waves throughout the 3 leads; very high pressure	Normal
R.S.	29	F	Severe retrosternal pain, from xiphoid to throat, lasting 10–15 seconds; 2 months duration; heavy psychosomatic component	Spontaneous spasm waves associated with pain	Normal

A third group is represented by 2 patients (Table III), in whom there was evidence of esophageal spasm during the roentgenographic evaluation, but no history of esophageal complaints. It is of interest to note that 1 of these patients was suffering from multiple sclerosis.

The fourth distinct category contains 11 patients (Table IV), in whom the symptomatology, manometry, and roentgenographic findings point towards classic idiopathic diffuse esophageal spasm. In this group a clear-cut, well defined group of symptoms was elicited which included painful dysphagia and regurgitation of long-standing duration. The patients were able to explain in their own words about the pain which varied from a sensation of discomfort beneath the lower half of the sternum to severe, sharp, substernal pain radiating into the neck and arms. The duration of symptoms spanned several years, the average being 6.5 years. Dysphagia was characterized by food sticking in the esophagus or collecting in the lower chest.

The presence of repetitive, simultaneous and often spontaneous contractions during the manometric studies was well documented in the entire group of patients (Fig. 1*B*).

The roentgenographic and fluoroscopic findings in the fourth group of patients

TABLE II

SECOND GROUP OF PATIENTS

	Age	Sex	Symptomatology	Manometric Findings	Roentgenographic and Fluoroscopic Findings
D.F.	64	F	"Thick phlegm in throat;" 2 years duration; hiatus hernia repair 9 months prior to admission with some relief of symptoms	Occasional spontaneous spasm waves with high amplitude and duration	Small hiatal hernia; spontaneous reflux; decreased motor function; delayed emptying of the esophagus
V.G.	19	M	Dysphagia for solids and liquids; 1 year duration	Absence of lower sphincter; absence of peristalsis, replaced by spasm waves	Complete motor failure; wide cardia and reflux
E.D.	59	M	Heart burn	Spontaneous and swallow induced spasm waves; Berstain test negative	Hiatus hernia; chronic peptic ulcer disease
P.D.	59	M	Intermittent inability to swallow; 4 years duration; retrosternal pain	Isolated spasm waves	Hiatus hernia; gastroesophageal reflux
B.R.	72	M	Substernal and epigastric burning 3 to 4 hours after going to bed, occasional dysphagia	Occasional repetitive contractions, some spontaneous; Berstain test positive	Hiatal hernia; poor propagation of the primary peristaltic wave
S.R.	52	M	History of dysphagia for 10 years; dilated 8 years ago with improvement	High amplitude spasm waves	Small hiatus hernia
A.J.	67	M	"Food sticking in throat;" 10 years duration	Spasm waves, intermittent with normal waves	Small hiatus hernia; reflux
H.A.	77	M	"Stomach trouble;" "difficulty in swallowing peanuts"	Spasm with swallowing; Mecholyl test positive	Decreased peristaltic activity; delayed emptying
O.L.	52	F	Intermittent "pressure like pain in the chest, radiating to the back"	Numerous spontaneous contractions; Berstain test positive with reproduction of pain	Prominent cricopharyngeus muscle; decreased peristaltic activity
D.H.	68	M	Epigastric pain aggravated by eating	Hypertonic lower esophageal sphincter with spasm; relief with nitroglycerin	Small hiatal hernia, delayed emptying
F.R.	50	F	Chest pain; heavy anxiety reaction	Simultaneous repetitive contractions during Berstain test; spasm waves	Small hiatal hernia

were those of slight dilatation of the upper third of the esophagus and replacement of the primary peristaltic esophageal wave in the lower two-thirds with simultaneous contractions producing the characteristic appearance of pseudodiverticula and delayed emptying (Fig. 2). Three patients had epiphrenic diverticulum (Fig. 3). Thickening of the esophageal wall was demonstrated roentgenographically and

TABLE III

THIRD GROUP OF PATIENTS

	Age	Sex	Symptomatology	Manometric Findings	Roentgenographic and Fluoroscopic Findings
L.R.	77	M	No history of gastrointestinal tract complaints; multiple sclerosis	Normal	Spasm
B.L.	57	M	No history of gastrointestinal tract complaints; chronic pancreatitis	Normal	Spasm

TABLE IV

FOURTH GROUP OF PATIENTS

	Age	Sex	Symptomatology	Manometric Findings	Roentgenographic and Fluoroscopic Findings
D.M.	48	F	Dysphagia; "food sticks in the esophagus;" duration 10 years; "no pain, but sensation of spasm in chest"	High pressure spasm waves with or without swallowing; complete lack of propulsive wave	Esophageal spasm; hypertrophy of the wall
R.I.	32	F	Dysphagia of 8 years duration; retrosternal pain; regurgitation	Spasm waves of high amplitude	Spasm documented for a period of 8 years
A.B.	39	F	Two year history of dysphagia; "food gets caught in lower chest," more difficulty with liquids; regurgitation	Spasm waves of high amplitude	Spasm; pulsion epiphrenic diverticulum; muscular hypertrophy demonstrated at surgery
S.S.	34	F	Dysphagia for 3 years; first noted with liquids; regurgitation; pain in anterior chest	Severe spasm waves	Spasm; muscular hypertrophy
G.C.	68	F	Dysphagia for 3 years; "food hangs up in the middle of the chest;" regurgitation	Simultaneous contractions and spasm waves	Spasm
W.P.	46	M	Dysphagia of 2 years duration; had hiatal hernia repair 1 year prior to admission; still symptomatic	Spontaneous, frequent spasm waves	Spasm
O.T.	69	F	"Food, liquids or solids seem to collect in the lower chest;" regurgitation for 15 years	Spasm waves	Spasm; muscular hypertrophy demonstrated at surgery
W.W.	81	M	Dysphagia-choking sensation; regurgitation for 15 years	Spasm waves	Spasm
B.W.	73	M	Feeling of food hanging up in the lower esophagus for 1½ years	Spasm waves in lower esophagus	Spasm; hiatal hernia
W.V.	82	M	History of dysphagia for 5 years	Spasm	Foreign body lodged in lower esophagus; spasm
M.M.	74	F	Difficulty of swallowing for 6 months, increasing in severity; able to swallow baby food only	Spasm	Neuromuscular dysfunction; spasm after aspiration; muscular hypertrophy at autopsy; muscular layer 8 mm. in thickness

proven either surgically or at autopsy in 4 patients (Fig. 4). It has been our experience that when the examination was repeated, the roentgenographic appearance was easily reproducible. This supports the observation of McNally and Katz[10] that once diffuse esophageal spasm is identified it can always be demonstrated thereafter.

DISCUSSION

In comparing the manometric findings with the roentgenographic findings, 4 groups of patients have been clearly identified.

Group I (Table I) represents patients in whom a manometric abnormality was present, but roentgenographic findings were absent. This group supports the concept that some patients may present with symptoms and manometry compatible with esophageal spasm, but without corresponding roentgenographic changes.[4]

Group II (Table II) probably represents patients in whom the manometric abnormality is secondary to esophagitis and gastroesophageal reflux. There is a high incidence of roentgenographically demonstrated hiatus hernia and reflux; there are few if any findings characteristic of esophageal spasm. This group of patients sup-

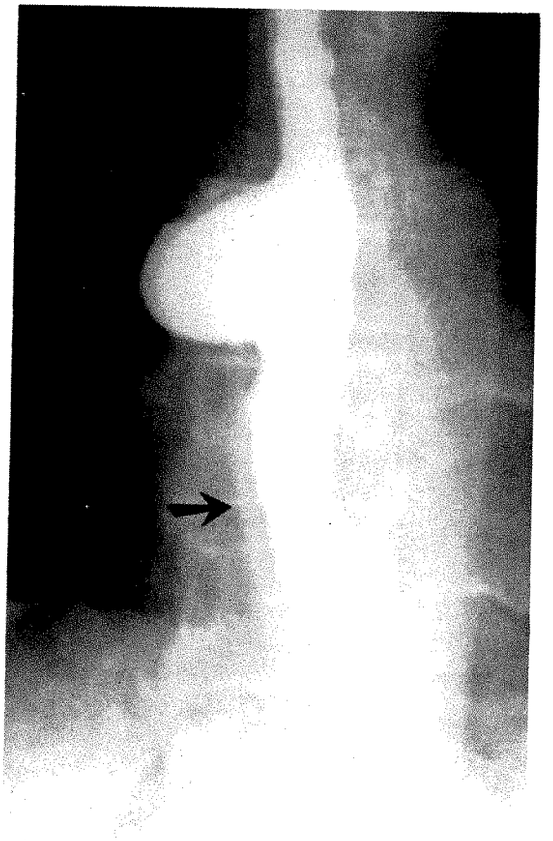


Fig. 3. Epiphrenic diverticulum. Evidence of esophageal wall thickening (arrow). Patient A.B. (Table IV). At surgery diffuse thickening of the wall of the lower esophagus was confirmed. Resection of the diverticulum and long submucosal myotomy were performed.

ports the thesis that the nonspecific, abnormal, motility pattern may be a manifestation of various disease processes.[2]

Two patients (Table III), although not of significant statistical value, may indicate that neuromuscular or central nervous system diseases may be the cause of the abnormal motility pattern.

Table IV represents a group of patients in whom the symptomatology, manometric data, and roentgenographic findings identify a distinct form of disease. The clinical manifestations are of long-standing duration and include dysphagia, regurgitation, choking, pain, and a sensation of foods collecting in the lower chest. The manometric findings (Fig. 1*B*) are well established and reproducible. Roentgenographic, fluoroscopic and cinefluoroscopic abnormalities can be demonstrated at any time once the syndrome is fully developed. Normal peristaltic waves move down through the esophagus to the level of the aortic arch at which point they are replaced by simultaneous repetitive contractions. Emptying of the esophagus is delayed. There is an increase in the thickness of the esophageal wall suggesting hypertrophy secondary to overfunction. Three instances of epiphrenic diverticulum were found confirming reports of the presence of pulsion diverticula proximal to areas of increased resistance to the flow of food.[1]

The foregoing strongly suggests that 3 well defined groups of patients may be encountered with "esophageal spasm." One patient group has esophageal spasm as a

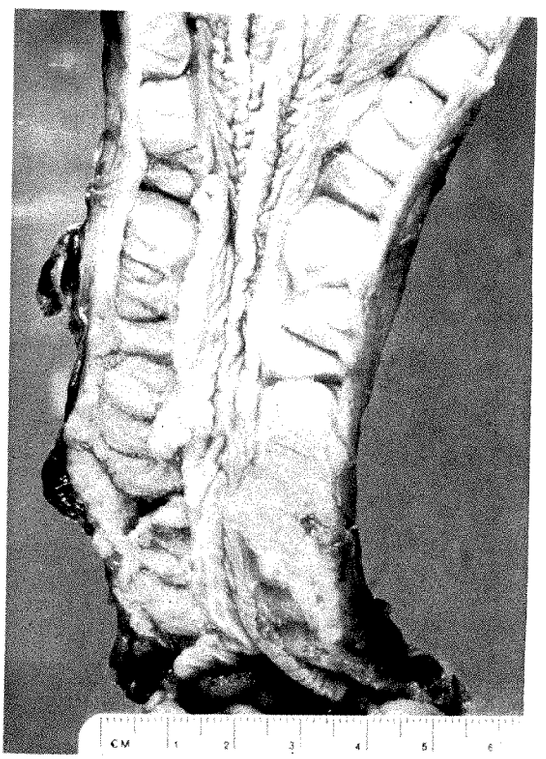


Fig. 4. Patient O.T. (Table IV). Photograph of the surgical specimen demonstrating the markedly hypertrophic muscular layer and contracted lumen. The colon was interposed.

manifestation of a disease process such as gastroesophageal reflux and esophagitis; and in the second the abnormal motility pattern may be secondary to the aging process or various central nervous system diseases. Finally, in a well defined group of patients, spasm is the manifestation of a primary disease process with a characteristic clinical history, and well documented manometric and roentgenographic findings.

The management of patients with diffuse esophageal spasm is intimately related to the underlying cause of abnormal motility. Therefore, a complete evaluation of the patient including a complete history and physical examination with neurologic evaluation, manometric studies, endoscopy, acid infusion test, measurement of the pH of the esophagus, fluoroscopy and cinefluoroscopy of the esophagus are required for an adequate diagnosis prior to the institution of any therapy. A team approach with very close cooperation between the radiologist and the gastroenterologist is not only desirable but indispensable in the diagnosis and management of these patients. The radiologist should be fully aware of the roentgenographic and fluoroscopic findings in all of the functional diseases that affect the esophagus. The roentgenographic evaluation should be conducted using a systematic approach with high quality fluoroscopy and cinefluoroscopy techniques.

If a diagnosis of hyperacidity with gastroesophageal reflux and esophagitis is made, it is the clinicians choice whether to treat the patient medically for hiatus hernia or to treat the patient with any of the multiple surgical procedures now available for the prevention of reflux.[11,15]

For cases of spasm due to old age, reassurance and an explanation of the benign nature of the disease process usually will be sufficient.

If idiopathic esophageal spasm is diagnosed and the symptoms are mild, with no significant deterioration in the health of the patient, management with tranquilizers and smooth muscle relaxants is probably satisfactory. On the other hand, if there is not complete relief of the symptoms and/or there is deterioration in the patient's condition, a surgical approach such as a long submucosal myotomy as proposed by Ellis *et al.*[5,6] may be indicated.

CONCLUSIONS

Diffuse esophageal spasm is a manifestation of disordered motility and may be secondary to acid irritation, to central nervous diseases or to the aging process. However, in a certain group of patients primary diffuse esophageal spasm associated with muscular hypertrophy appears to be an independent clinical entity in which the diagnosis is well established by clinical, manometric and roentgenographic findings.

The specific nature of the origin of the esophageal spasm must be clearly defined prior to the undertaking of any therapy.

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MULTIPLE LEIOMYOMAS OF THE ESOPHAGUS*

By JOSEPH E. GODARD, M.D.,† *and* DOLPH McCRANIE, M.D.
OKINAWA

ALTHOUGH leiomyoma of the esophagus is a relatively uncommon lesion, it is by far the most frequent benign tumor which involves this structure. Moersch and Harrington[8] could find only 44 benign tumors of the esophagus in 7,459 autopsies done at the Mayo Clinic, but 32 (73 per cent) of these were leiomyomas. In a series of 103 benign esophageal tumors obtained equally from surgical and autopsied patients, Totten *et al.*[15] found 46 (45 per cent) to be leiomyomas.

Over 500 cases of leiomyoma of the esophagus have been reported in the world literature to date,[5] but we could find only 20 instances in which multiple tumors existed.[2–4,7,9,11,14]

The purpose of this paper is to report an additional case of multiple leiomyomas of the esophagus and to review its salient clinical and roentgenographic features.

CLINICAL FEATURES

Age and Sex Incidence. Approximately 90 per cent of esophageal leiomyomas are found between the ages of 20 and 60 years. The peak surgical incidence occurs in the third and fourth decades, indicating that symptomatic tumors are confined primarily to early adult and middle life. The tumors have a slight predilection for the male sex, with some series reporting ratios as high as 2:1.

Location. Approximately 60 per cent of leiomyomas occur in the lower third of the esophagus, 33 per cent in the middle third and 7 per cent in the upper third.[13] Their relative rarity in the upper esophagus reflects its smaller amount of smooth muscle.

Symptoms. About 50 per cent of patients remain asymptomatic—a figure attested to by the large number of tumors found incidentally at autopsy. Varying degrees of dysphagia and substernal pain are the most common presenting symptoms. Size and growth characteristics of the tumor are the most important factors in the production of symptoms. Reviews of surgically treated cases suggest the average size of symptomatic tumors to be 6–8 cm. and tumors twice this size are not uncommon. Esophageal leiomyomas grow slowly and usually produce intermittent, insidiously progressive symptoms. Occasionally, they will encircle the esophagus in a serpentine or U-shaped fashion and cause obstructive symptoms. Bleeding is not characteristic, since the tumor is a predominantly *intramural* lesion and rarely causes ulceration of the overlying mucosa.

Malignant Potential. Leiomyomas of the esophagus are benign smooth muscle tumors which have little, if any, tendency to undergo malignant degeneration. To our knowledge, there has been only 1 report of a tumor diagnosed histologically as a "fibroleiomyoma," which contained a small focus of leiomyosarcoma.[1]

Esophagoscopy. The esophagoscopic findings may be completely negative due to easy passage of the instrument past the tumor. More typically, a firm submucosal mass with normal or flattened overlying mucosa may be seen to indent the lumen of the esophagus. The chief value of esophagoscopy is to exclude a mucosal tumor. Biopsy through an intact, healthy mucosa is contraindicated.

Treatment. Thoracotomy and simple enucleation is the treatment of choice in the majority of cases. Occasionally, a tumor will be so extensive or adherent as to require resection and esophagogastrostomy. This is particularly true when the lesion

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The views expressed in this paper are those of the authors and do not reflect the views of the United States Army or Department of Defense.
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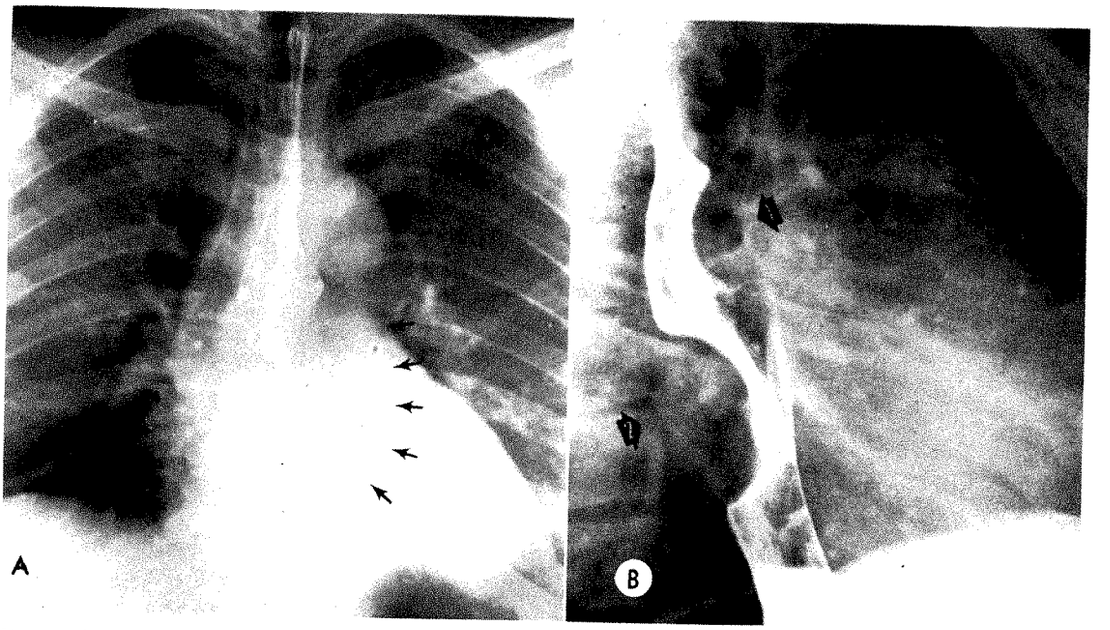


FIG. 1. Barium esophagograms. (*A*) "Forked-stream" appearance due to splitting of barium column by tumor, nonobstructing narrowed segment, and large smooth retrocardiac mass (arrows) are seen in the anteroposterior erect view. (*B*) Lateral roentgenogram shows 2 large, sharply-demarcated, crescentic filling defects with shelving at upper and lower margins.

involves the esophagogastric junction. Tumor recurrence following surgery is extremely rare.

ROENTGENOGRAPHIC FEATURES

The correct preoperative diagnosis of esophageal leiomyomas is greatly dependent upon their recognition by the radiologist. Fortunately, these tumors have a fairly characteristic appearance on barium swallow examination. The roentgenographic features of benign intramural tumors have been described in detail by Schatzki and Hawes,[10] and by Harper and Tiscenco.[6]

Classically, there is a smoothly rounded or crescent-shaped filling defect in the barium column when the esophagus is viewed in profile. Sharp demarcation between the tumor edges and the uninvolved esophagus is characteristic. A sudden "step" or "shelf" in the lumen with abrupt angulation at the upper and/or lower margins of the tumor is frequently seen in the lateral roentgenogram. A smooth or lobulated companion soft tissue mass opposite the filling defect can usually be demonstrated. The overlying mucosal folds may be normal, or, in the case of a large tumor may be stretched and flattened, producing a "smear effect." When studied *en face*, the barium column may sometimes be split to either side of the tumor, producing a "forked-stream" appearance. The esophagus may also appear narrowed at the tumor site when viewed *en face*, but no obstruction to flow of barium is seen. On fluoroscopy, esophageal motility is normal and the soft tissue mass is seen to move with the esophagus on deglutition. Calcification within the tumor mass is unusual but has been occasionally reported.[7,16]

Although barium examination usually permits an accurate diagnosis, other diagnoses such as esophageal varices, cardiospasm, double aortic arch, paraesophageal hiatal hernia, duplication cyst of the esophagus and extrinsic mediastinal tumors are not uncommonly suggested by the radiologist. The most frequent diagnostic error made is that of cardiospasm because of transient esophageal dilatation and mis-

interpretation of the tumor mass as retained secretions or food. It should be emphasized that careful fluoroscopic examination usually permits differentiation from these other conditions.

REPORT OF A CASE

A 28 year old Negro male was admitted to the hospital with the chief complaint of mild, intermittent dysphagia of 3 months' duration. Barium swallow examination revealed 2 large, sharply-demarcated, crescentic filling defects of the middle and lower esophagus (Fig. 1, *A* and *B*). A large smooth soft tissue mass opposite the filling defects was evident and moved freely with the esophagus during deglutition. Esophageal motility and pliability were normal and barium passed with ease through the involved areas (Fig. 2, *A–D*). Esophagoscopy showed a firm submucosal mass which indented the esophagus at 32 cm. from the upper incisors.

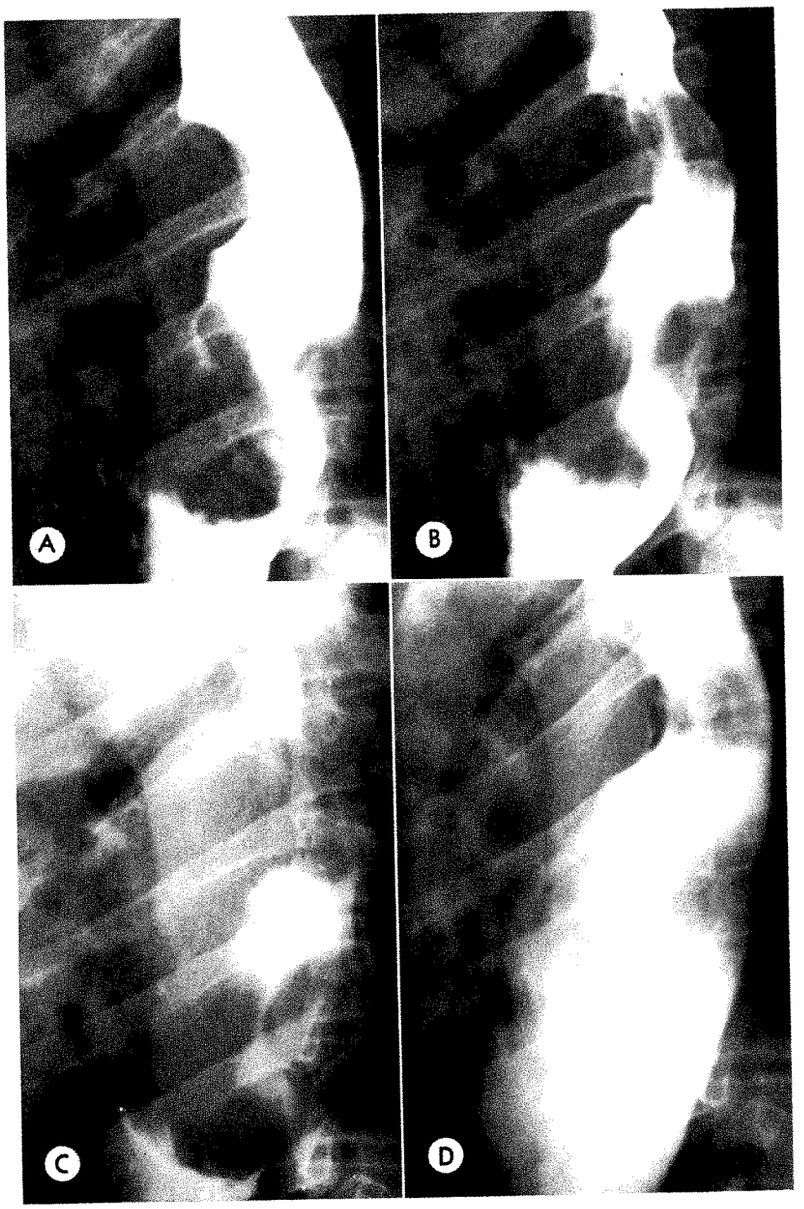


FIG. 2. (*A–D*) Sequential spot roentgenograms showing normal esophageal motility and pliability. Companion soft tissue tumor masses are seen opposite to filling defects.

The esophagoscope could be passed for only an additional 5 cm. beyond the tumor.

Exploratory thoracotomy revealed a large, firm intramural tumor of the lower third of the esophagus and a smaller second tumor at the level of the mid-esophagus, immediately behind the pulmonary hilum. The smaller lesion was approximately 2 cm. above the highest extent of the lower lesion and measured 4.6×1.7 cm. The larger lesion serpentined around the lower esophagus and measured 11.0×3.3 cm. The tumors were well-encapsulated and enucleation of both was accomplished without difficulty.

Histologic examination showed both tumors to be benign leiomyomas.

SUMMARY

Leiomyoma is the most common solid benign tumor of the esophagus.

Although leiomyomas are usually solitary, multiple tumors occur in about 4 per cent of cases.

A patient with 2 separate leiomyomas of the esophagus is reported and the clinical and roentgenographic features of esophageal leiomyomas are reviewed.

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ROENTGEN SIGNIFICANCE OF THE DUODENOCOLIC RELATIONSHIPS: AN ANATOMIC APPROACH*

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THE precise anatomic relationships between the duodenal loop and the transverse colon are often of critical importance in the roentgenologic interpretation of upper abdominal pathology. Their points of most intimate relationship represent anatomic crossroads between intraperitoneal and extraperitoneal structures and thus permit specific localization and diagnosis of a disease process. Because of this relationship, a lesion originating in one may have its major effect on the other. Particularly if roentgenologic investigation is initiated by a study which manifests the striking secondary effects, the presentation of findings may then be very misleading until the nature of the relationship and the primary site are appreciated.

The purpose of this report is twofold: (1) to clarify the intimate relationships of the transverse colon, transverse mesocolon and duodenum; and (2) to document the practical application of these anatomic features in the roentgenologic diagnosis of a variety of abdominal disease states involving these relationships.

MATERIAL AND METHOD

Cadavers were frozen to a solid state by placing them in a tank of dry ice for 36 hours. They were then cut on a band saw in horizontal and sagittal sections of approximately 1½ inch thickness. The sections were studied and photographed and the anatomic relationships established.

Selected clinical cases in which the duodenocolic relationships were involved in a variety of disease processes were reviewed and the roentgenographic changes correlated with the surgical and pathologic findings.

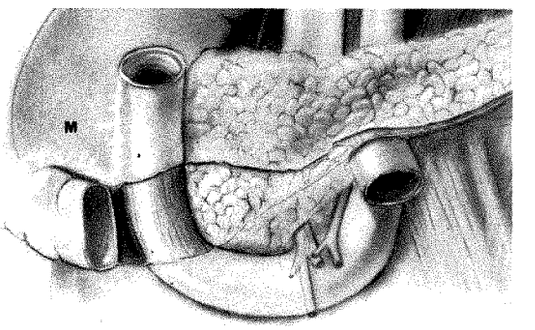


FIG. 1. Drawing showing the root of the transverse mesocolon, extending across the infraampullary portion of the duodenum and the lower border of the pancreas. Note the relationships of the anterior hepatic flexure of the colon and of the duodenojejunal junction. M marks the location of Morison's pouch, the intraperitoneal posterior extension of the right subhepatic space.

ANATOMIC AND NORMAL ROENTGENOGRAPHIC FEATURES

The key to understanding the significance of the duodenocolic relationships is the insertion of the root of the transverse mesocolon and its planes of reflection (Fig. 1).

Characteristically, the "hepatic flexure" of the colon is composed of 2 curvatures.[7] The proximal, more posterior one continues from the fixed extraperitoneal ascending colon and is related to the inferior and lateral edge of the right kidney and the posterolateral tip of the liver. The colon then passes immediately anteromedially over the descending duodenum to the second curve of the hepatic flexure, which is more anterior and superior and is related to the gallbladder.

At a point between the 2 curvatures of

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FIG. 3. Right paramedian sagittal section at the level of the duodenal bulb (DB) and the descending duodenum (DD), showing their relationship to the anterior hepatic flexure (AHF) of the colon before it continues ventrally as the transverse colon (TC). The dashed line indicates the transverse mesocolon.



FIG. 2. Transverse section through the right abdomen at the level of the duodenal bulb (DB) and the proximal descending duodenum (DD). Note the intimate relationship of the hepatic flexure of the colon (C) at the beginning reflection of the transverse mesocolon. ST, stomach; gb, gallbladder; L, liver; K, right kidney.

the hepatic flexure as the colon is in intimate relationship to the descending duodenum, it begins to pick up the peritoneal sling of the transverse mesocolon. The colon in this area is then in virtual contiguity with the second portion of the duodenum, with the very short edge of the beginning reflection of the transverse mesocolon providing a fascial plane (Fig. 2; and 3).

The root of the transverse mesocolon, after broadly intersecting the infraampullary portion of the descending duodenum, continues along the anterior surface of the

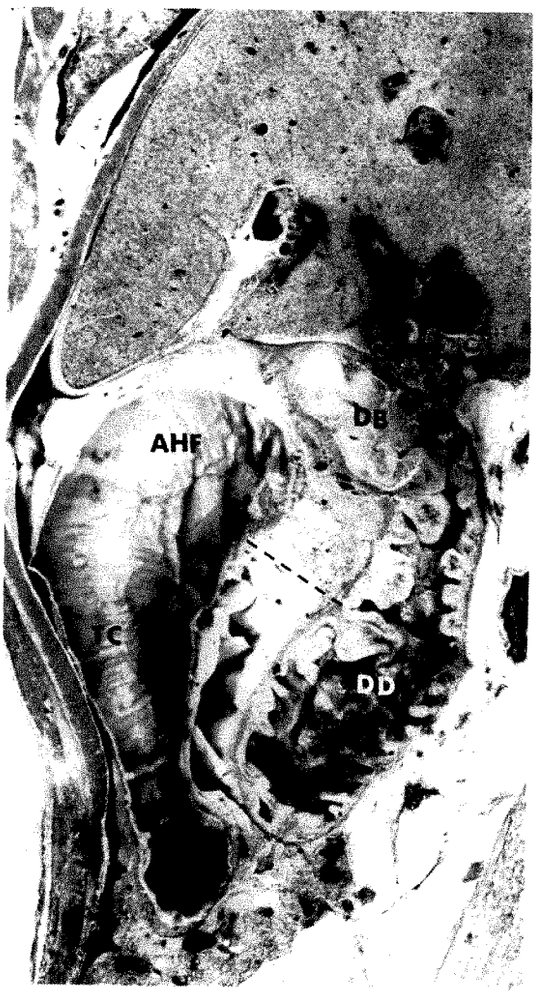




FIG. 4. Left parasagittal section at the level lateral to the duodenojejunal junction. Shown are the relationships of the proximal jejunal loops (J) to the transverse colon (TC) and its mesocolon (arrowheads), coursing along the inferior aspect of the tail of the pancreas (P). The section is also through the spleen (S) and left kidney (K).

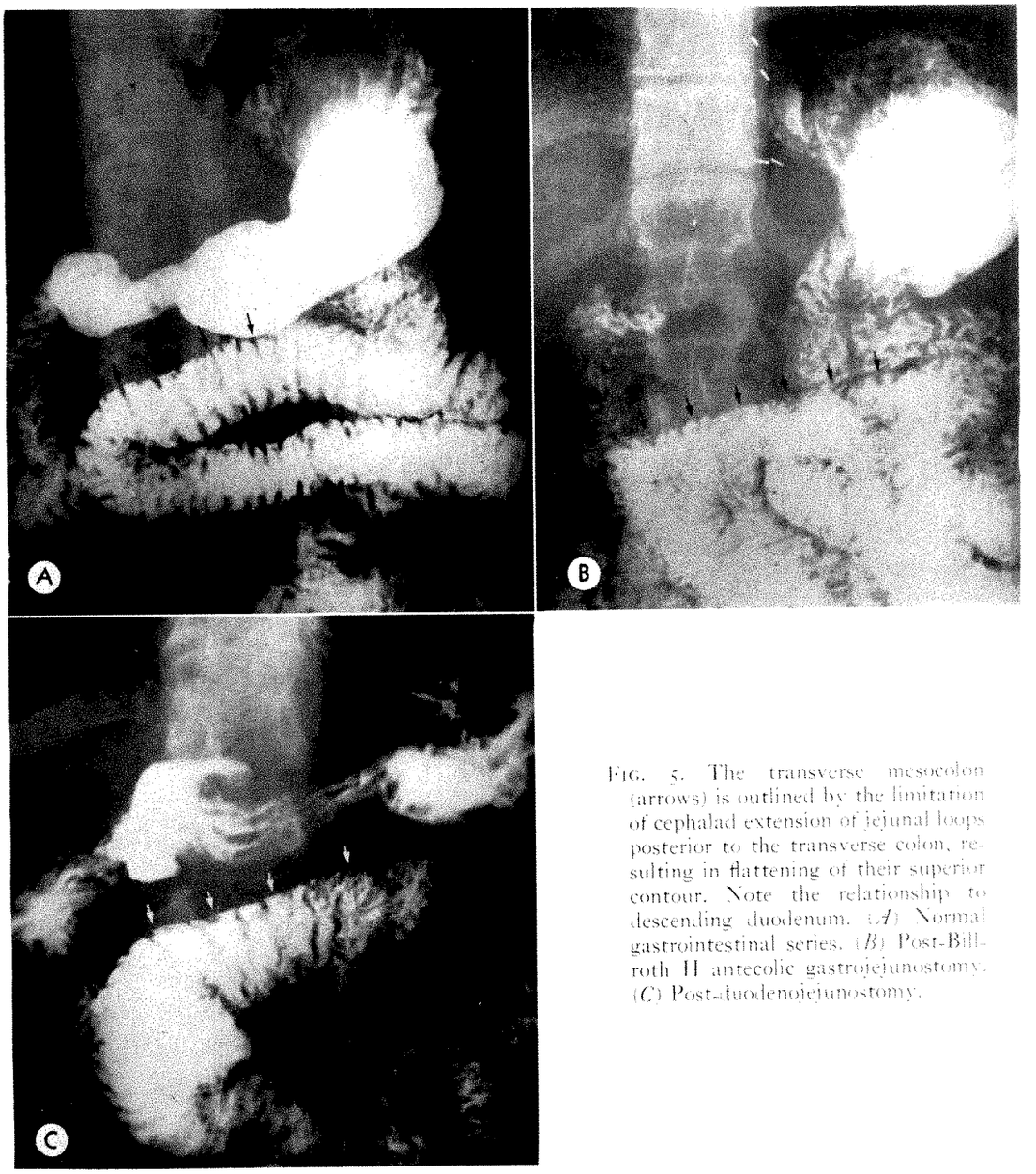


Fig. 5. The transverse mesocolon (arrows) is outlined by the limitation of cephalad extension of jejunal loops posterior to the transverse colon, resulting in flattening of their superior contour. Note the relationship to descending duodenum. (*A*) Normal gastrointestinal series. (*B*) Post-Billroth II antecolic gastrojejunostomy. (*C*) Post-duodenojejunostomy.

pancreas, being attached to the mid-portion of the head and the inferior surface of the body and tail. The nonperitonealized bare area, wide on the right and progressively thinner toward the left, thus provides a shared anatomic fascial plane between the pancreas and descending duodenum behind and the transverse colon in front, along the leaves of the transverse mesocolon.

The transverse mesocolon itself is a fan-shaped structure in the horizontal plane of the body. Short at its beginning, it is longest in the mid-sagittal plane to become abbreviated laterally again as the colon comes in relationship to the left kidney and spleen. The length of the transverse mesocolon is variable. It tends to be short in stocky individuals and long in tall, thin patients.

The retroperitoneal duodenum bends

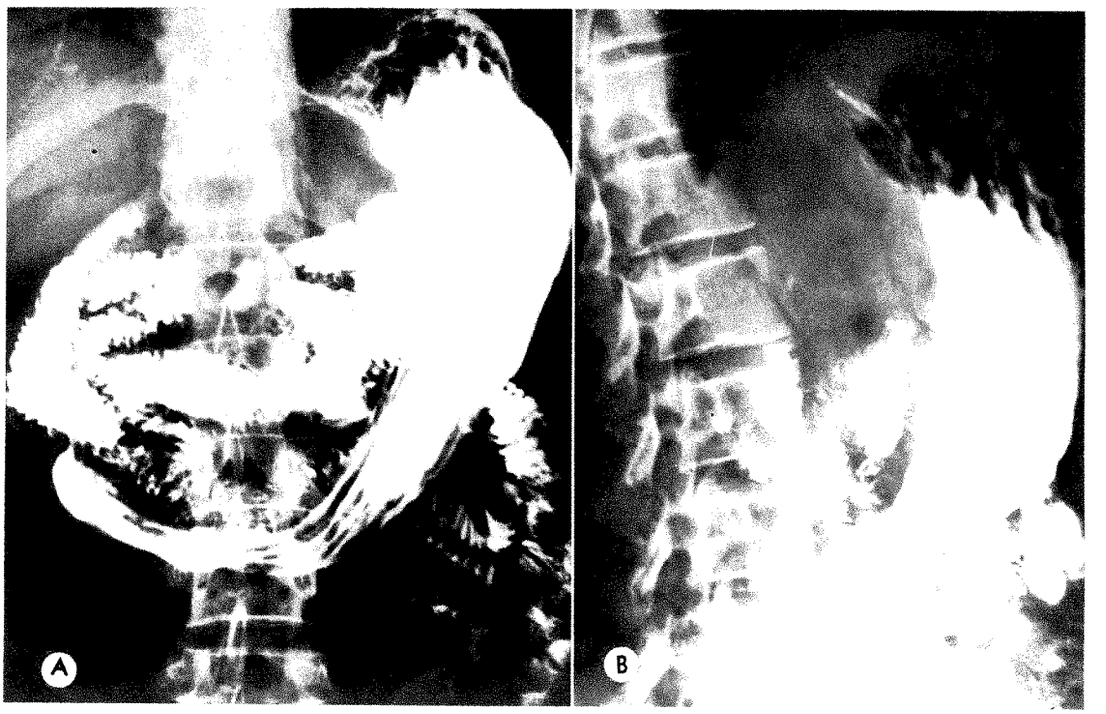


FIG. 6. Internal hernia into the lesser sac through a large defect in the transverse mesocolon. This is indicated by the high position of the loops of small bowel above the normal insertion of the transverse mesocolon which no longer determines their contour. (*A*) Frontal roentgenogram. (*B*) Prone oblique roentgenogram. Note that the herniated loops present posterior to the transverse colon and stomach. (Courtesy of E. Robert Heitzman, M.D., S.U.N.Y. Upstate Medical Center, Syracuse, New York.)

forward after its ascending portion at the level of the ligament of Treitz to penetrate the posterior parietal peritoneum and continue as the intraperitoneal jejunum. The duodenojejunal junction is then in intimate relationship to the inferior reflection of the transverse mesocolon (Fig. 1; and 4). It also serves as a useful landmark for dividing the body and tail of the pancreas.

The duodenojejunal junction, fixed by the ligament of Treitz, generally maintains its position throughout life at the approximate level of the lower border of L-1. With progressive laxity of support, however, the duodenal bulb and proximal portion of the second duodenum tend to descend with age, most marked in the fifth and sixth decades.[1] Nevertheless, the position of the root of the transverse mesocolon, which separates the peritoneal cavity from the lesser sac, can be constantly indicated on an upper gastrointestinal series by a line drawn from the infraampullary segment of the descending duodenum to a point immediately above the duodenojejunal junction. This delimits the most superior ascent of small bowel loops posterior to the transverse colon normally possible (Fig. 5).

On the right, the colon inferiorly and the descending duodenum medially provide 2 of the boundaries of the posterior intraperitoneal extension of the subhepatic space (Morison's pouch) anterior to the kidney (Fig. 1).

ROENTGEN PATHOLOGIC FEATURES

DEFECT OF MESOCOLON

On occasion, jejunal loops may normally present within the upper abdomen anterior to the transverse colon and perhaps the stomach. Cephalad extension of small bowel loops *posterior* to the transverse

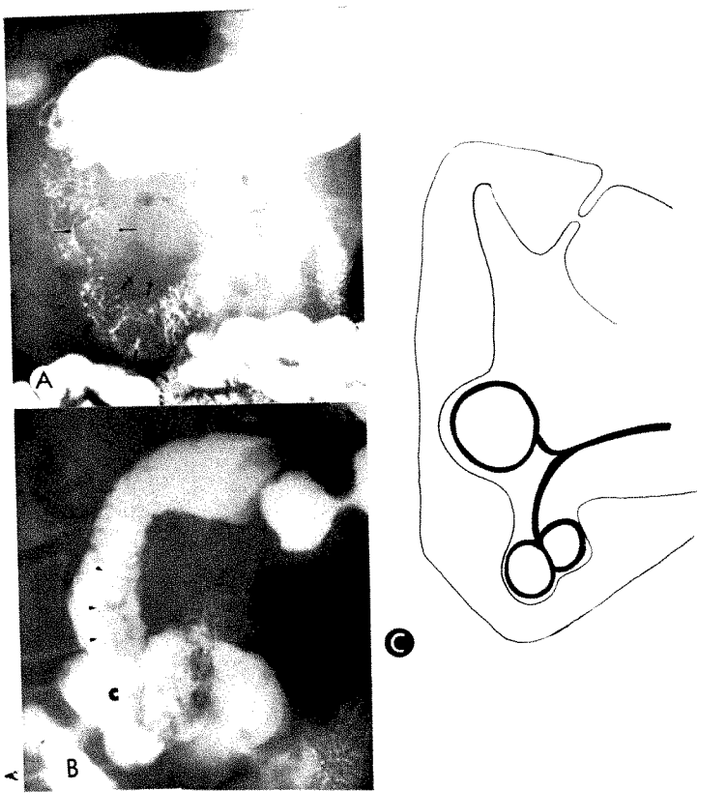


Fig. 7. Lymphangitic cysts within the leaves of the transverse mesocolon producing extrinsic nodular indentations upon the descending duodenum. (*A*) Prone roentgenogram. Three discrete mass impressions are shown (arrows). (*B*) Right lateral projection. The larger, more proximal indentation presents on the anterior aspect of the descending duodenum (arrowheads). Note its relationship to the hepatic flexure of the colon. (*C*) Diagram of the cysts within the mesocolon leaves bridging the bare area of the descending duodenum.

colon above the line of the root of the transverse mesocolon in relationship to the descending duodenum and duodenojejunal junction indicates a defect of that mesentery with internal herniation into the lesser sac (Fig. 6, *A* and *B*).

Masses within Mesocolic Leaves

Pathologic alteration in the contour of the duodenum by a localized abnormality arising in the origin of the reflections of the transverse mesocolon is shown in Figure 7, *A–C*. The bare area is widest at this site so that symmetric growths developing within the leaves may impress upon the duodenum over a considerable length. The typical points of pressure, then, are at the immediate infraampullary and the genu locations.

Effect on the Descending Duodenum by Carcinoma of the Hepatic Flexure

It is not generally appreciated that changes in the duodenal loop may be secondary to a carcinoma of the hepatic flexure of the colon.[6] The virtual contiguity of the 2 structures and the intervening short fascial plane of the transverse mesocolon allow ready spread of an inflammatory or neoplastic process. The occult nature of carcinoma of the right colon is well known and the palpation of an epigastric mass may lead the clinician to suspect the upper gastrointestinal tract. In such cases, if roentgenologic investigation is initiated by an upper gastrointestinal series, the resulting change in the descending duodenum with extrinsic pressure defects from en-

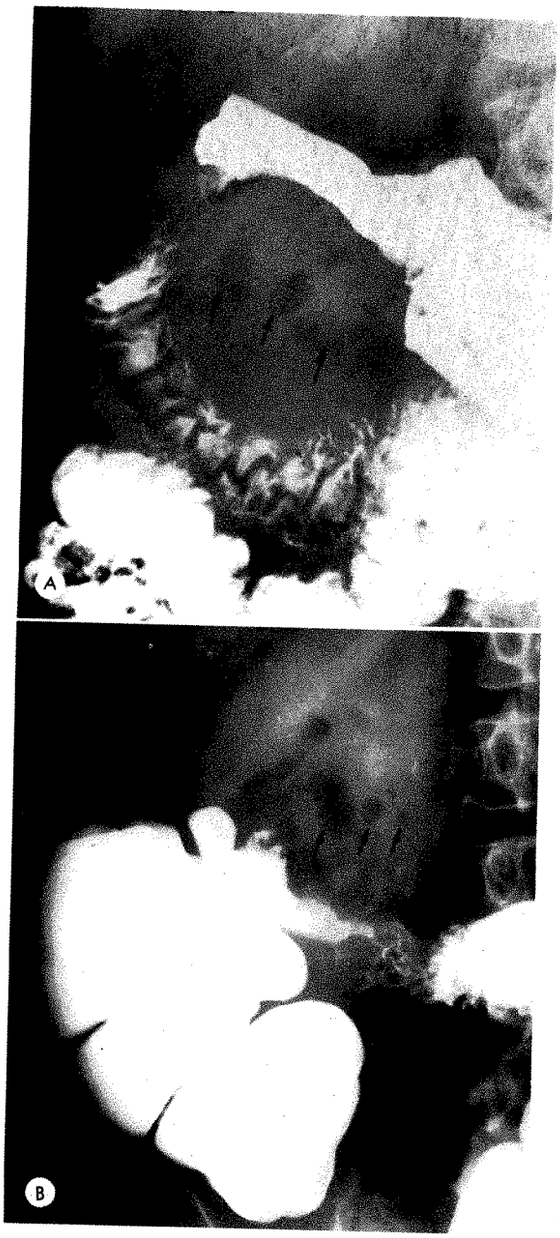


FIG. 8. Extension of colonic carcinoma across the mesocolon to the paraduodenal area. (*A*) Upper gastrointestinal series reveals numerous gas-containing abscess cavities (arrows) within a mass in the area of the head of the pancreas. There is edema and distortion of the mucosal folds of the descending duodenum. (*B*) A subsequent barium enema study shows a primary infiltrating carcinoma of the anterior hepatic flexure with a pericolonic-paraduodenal abscess. (Reproduced with permission of the *British Journal of Radiology*.[6])

larged lymph nodes and occasionally associated gas-containing cavities raises the possibilities of such conditions as a pancreatic carcinoma, pancreatic abscess, or leiomyosarcoma of the duodenum. These considerations may be very misleading until a barium enema examination is pursued and the primary site revealed (Fig. 8, *A* and *B*). After extension of the process from the colon to the duodenum, spread may occur beyond the limits of the mesocolon.

EFFECT ON THE COLON FROM A MASS ARISING IN THE DESCENDING DUODENUM

It has been shown that the distal hepatic flexure is in intimate relationship posteriorly to the descending duodenum. Localized anterior displacement of this portion of the colon then indicates a mass arising not in the nearby right kidney or gallbladder but specifically in the second portion of the duodenum (Fig. 9, *A* and *B*). Following identification of the displacement on an initial barium enema study, roentgenologic investigation can then be immediately directed to the primary site.

INFRAMESOCOLIC EXTENSION OF NEOPLASM OF THIRD DUODENUM

The third portion of the duodenum lies retroperitoneally below the root of the transverse mesocolon. Extension of a mass arising in this structure is then revealed on barium enema examination by characteristic elevation of the proximal transverse colon (Fig. 10*A*). While this type of displacement may occur secondary to such conditions as mesenteric cysts or primary retroperitoneal tumors, initial identification of this inframesocolic component should lead to careful investigation of the transverse duodenum (Fig. 10*B*).

ACUTE PANCREATITIS

Several of the plain film roentgenographic changes associated with acute pancreatitis, while strongly suggestive of the diagnosis, are by no means pathognomonic. Ileus of the transverse colon in a pattern



FIG. 9. Leiomyosarcoma of second portion of duodenum with large extramural component. (*A*) Right latera barium enema roentgenogram shows anterior displacement of the distal hepatic flexure of the colon (arrow) (*B*) Upper gastrointestinal series then reveals narrowing, large ulceration and mass effect upon the descending duodenum (arrows).

approaching the "colon cut-off" sign may be seen in a variety of conditions.[3] "Sentinel-loop" dilatation of the descending duodenum may occur secondary to acute cholecystitis or acute right perinephritis. However, simultaneous paralytic dilatation of both, secondary to the effects of the extravasated enzymes along the shared fascial planes, is diagnostic of acute pancreatitis (Fig. 11).

ABSCESS OF MORISON'S POUCH VS. INFRAMESOCOLIC ABSCESS

The point of juncture between the hepatic flexure and its mesocolon inferiorly and the descending duodenum medially provides 2 of the anatomic boundaries of Morison's pouch. This peritoneal recess is the posterior extension of the right subhepatic space. Secondary to the pathways of spread and localization of acute intraperitoneal exudates, it is the commonest site of an intraabdominal abscess.[4] Distinction of a gas-containing abscess of Morison's pouch from such conditions in the right upper quadrant as emphysematous cholecystitis, renal or perirenal abscess, liver abscess, and an anterior abdominal wall abscess can be easily made with recognition of its precise duodenocolic boundaries (Fig. 12).

The duodenocolic relationships are of further significance in localizing an abscess to the infracolic space, observations which may lead to identification of its site of origin. Figure 13, *A–C*, illustrates an abscess also relating to the duodenum and colon in a patient with an automobile lap-belt deceleration injury. While it lies anterior and primarily lateral to the descending duodenum in the plane of Morison's pouch (Fig. 13*A*), it is not until its inframesocolic position is documented that its source from a ruptured jejunal loop is ascertained (Fig. 13*B*).

DUODENOJEJUNAL JUNCTION: RELATION TO COLON

The intimate relationship of the duodenojejunal junction superiorly to the root of the transverse mesocolon as it extends across the pancreas is of importance in the identification of both locally arising processes and remote colonic pathology.

At this level, the mesocolon is generally of sufficient length so that the transverse colon is considerably anterior. It is then

FIG. 11. Acute pancreatitis. The roentgenologic finding of associated ileus of the transverse colon and of the descending duodenum (shown here by stasis of barium within the dilated loop) is diagnostic of this condition.

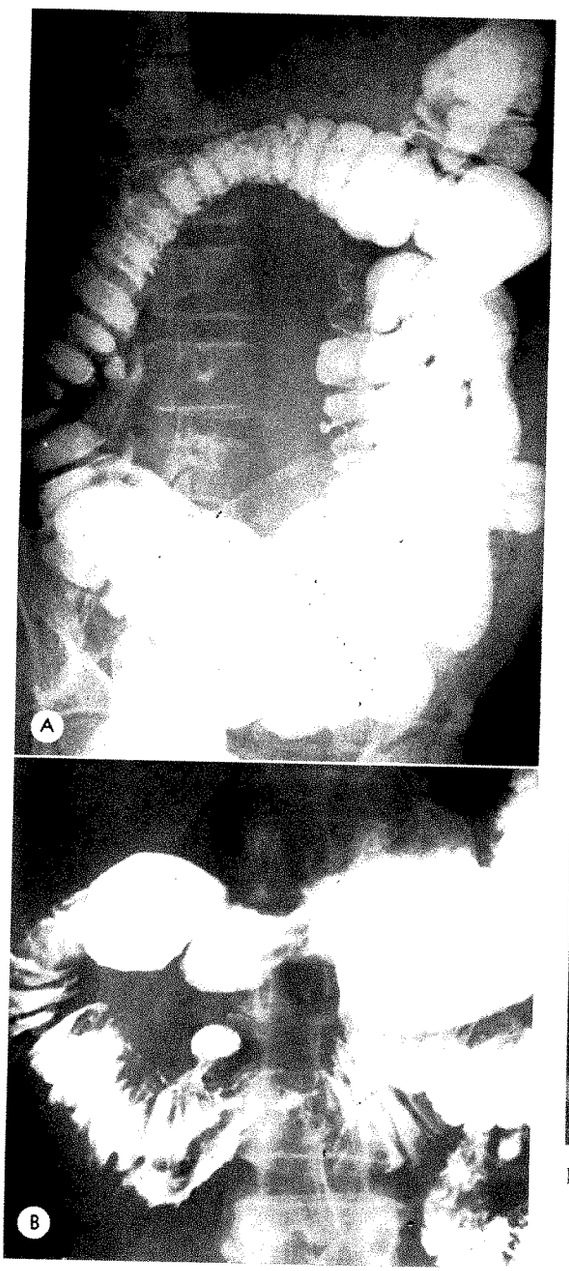


FIG. 10. Leiomyosarcoma of third portion of the duodenum with large extramural component. (*A*) There is gross elevation and displacement of the proximal transverse colon by a huge mass. (*B*) Upper gastrointestinal series documents the changes of leiomyosarcoma arising in the transverse duodenum, characterized by irregular ulcerations and sinus tracts within a lobulated and serpiginous submucosal tumor. (Reproduced with permission of *Clinical Radiology*.[5])

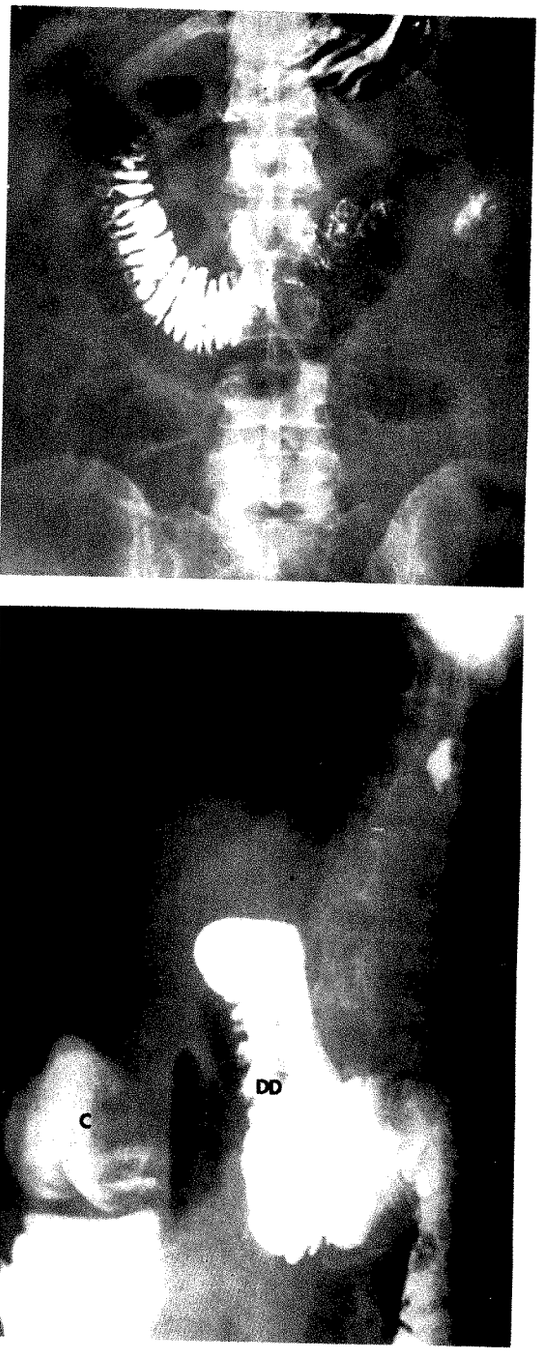


FIG. 12. Abscess of Morison's pouch. Right lateral decubitus projection. Margination by the descending duodenum (DD) medially and the hepatic flexure of the colon (C) inferiorly and laterally localizes the gas and fluid-containing abscess specifically to the posterosuperior recess of the subhepatic space (Morison's pouch).

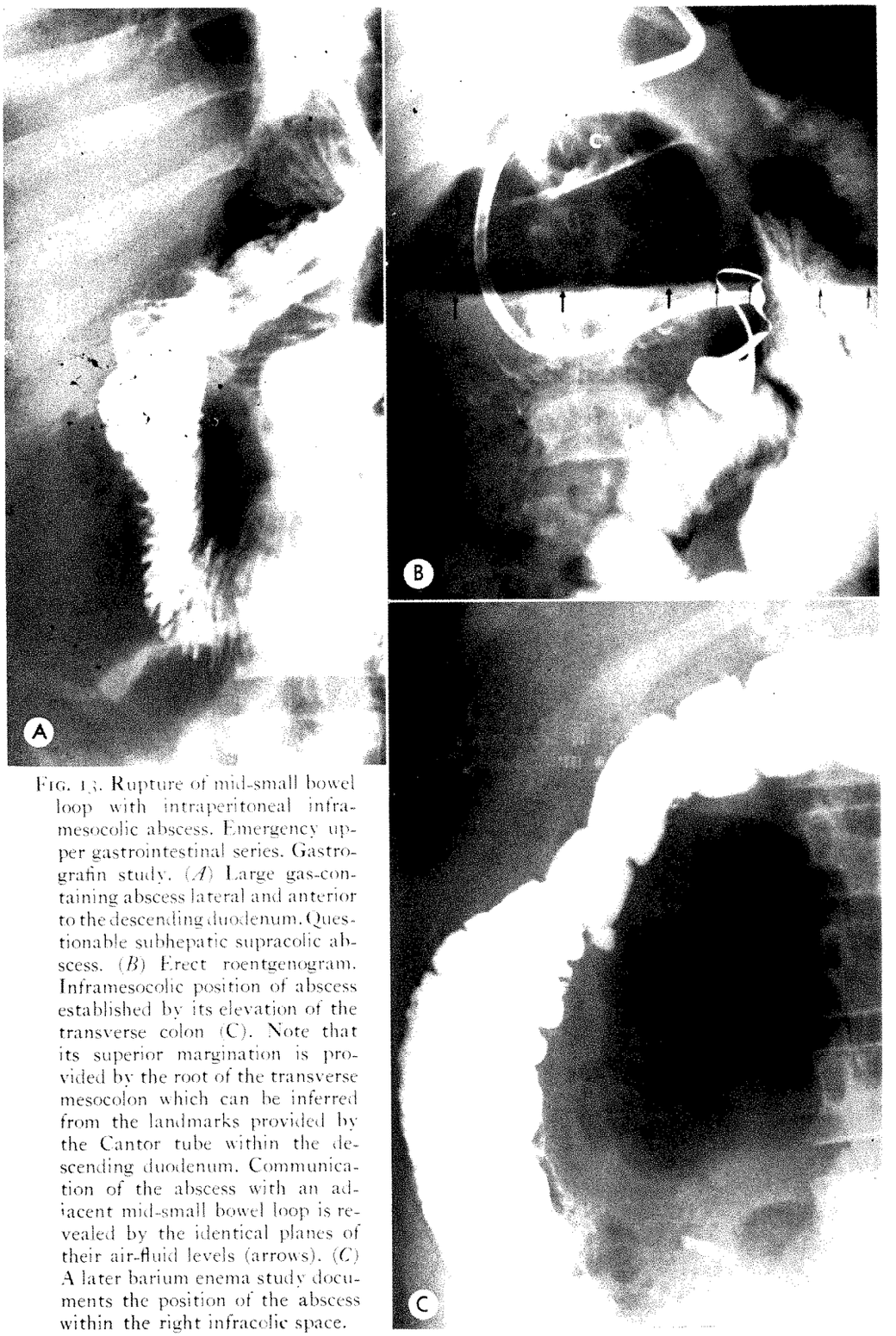


FIG. 13. Rupture of mid-small bowel loop with intraperitoneal inframesocolic abscess. Emergency upper gastrointestinal series. Gastrografin study. (*A*) Large gas-containing abscess lateral and anterior to the descending duodenum. Questionable subhepatic supracolic abscess. (*B*) Erect roentgenogram. Inframesocolic position of abscess established by its elevation of the transverse colon (C). Note that its superior margination is provided by the root of the transverse mesocolon which can be inferred from the landmarks provided by the Cantor tube within the descending duodenum. Communication of the abscess with an adjacent mid-small bowel loop is revealed by the identical planes of their air-fluid levels (arrows). (*C*) A later barium enema study documents the position of the abscess within the right infracolic space.

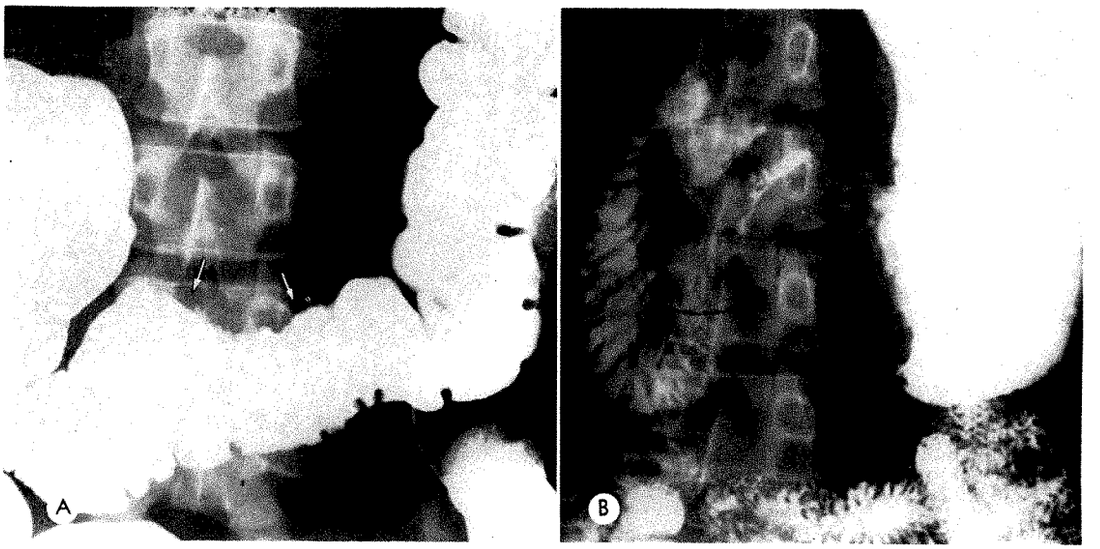


FIG. 14. Cyst of the posterior parietal peritoneum below the root of the mesocolon. (*A*) Mild extrinsic pressure effect upon the superior contour of the transverse colon (arrows). (*B*) Gross medial displacement of the fourth portion of the duodenum and duodenojejunal junction, with pressure upon the greater curvature of the gastric antrum.

apparent that minor effects on the distal transverse colon on an initial barium enema study may be shown to reflect a process that predominantly involves the ascending duodenum or duodenojejunal junction (Fig. 14, *A* and *B*; and 15, *A* and *B*).

By its relationship to the central lymph nodes draining the colon, the duodenojejunal junction may reflect changes of lymph node spread from a remote carcinoma of the colon. The lymphatic vessels draining the colon parallel the arterial

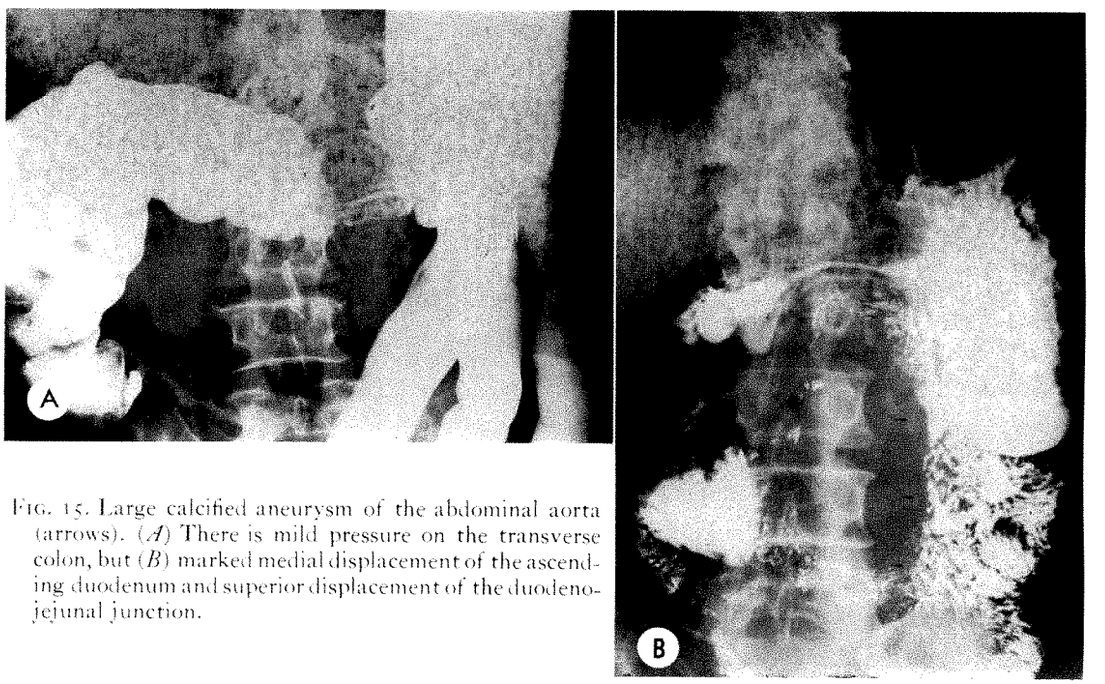


FIG. 15. Large calcified aneurysm of the abdominal aorta (arrows). (*A*) There is mild pressure on the transverse colon, but (*B*) marked medial displacement of the ascending duodenum and superior displacement of the duodenojejunal junction.

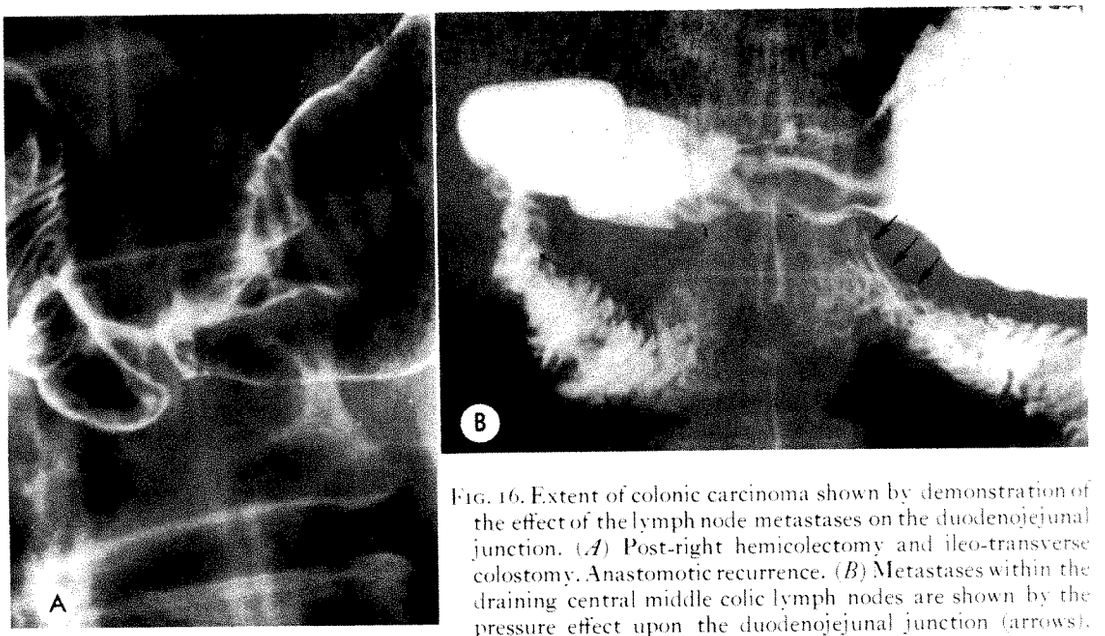


FIG. 16. Extent of colonic carcinoma shown by demonstration of the effect of the lymph node metastases on the duodenojejunal junction. (*A*) Post-right hemicolectomy and ileo-transverse colostomy. Anastomotic recurrence. (*B*) Metastases within the draining central middle colic lymph nodes are shown by the pressure effect upon the duodenojejunal junction (arrows). The mass of the recurrent neoplasm itself has also produced a pad effect upon the adjacent gastric antrum.

supply. The central lymph nodes lie in relation to the duodenal loop. Those draining the right side of the colon are located near the origin of the superior mesenteric artery, in close relationship to the third portion of the duodenum. Those draining the distal transverse colon and descending colon are located in the transverse mesocolon and near the ascending left colic artery which courses *lateral* to the fourth portion of the duodenum.



FIG. 17. Pressure effect upon the superior contour of the duodenojejunal junction by early carcinoma of the body of the pancreas. There is flattening and a double contour (arrows).

McCort[2] has shown roentgenologically that by recognizing changes in the third portion of the duodenum from enlargement of the central superior mesenteric lymph nodes in the drainage pathway of the right side of the colon, it may be possible to determine the extent of a right colonic carcinoma preoperatively or the development of lymph node metastases postoperatively.

In a similar manner, we have observed that involvement of the lymph nodes draining the distal half of the transverse colon and the descending colon may be revealed by pressure effects upon the *lateral* aspect of the duodenojejunal junction. Figure 16, *A* and *B*, illustrates an anastomotic neoplastic recurrence at the site of a previous ileo-transverse colostomy. Extension is clearly shown by the effects of lymph node spread upon the lateral contour of the duodenojejunal junction. This change is distinct from that produced by a mass arising within the adjacent pancreas. This typically results in flattening of the normally

convex superior contour of the duodenojejunal junction (Fig. 17).

SUMMARY

A knowledge of the intimate relationships between the transverse colon, transverse mesocolon and duodenum is often of critical importance in the roentgen analysis of upper abdominal pathology. Detailed study of their anatomic relationships was made by sections derived from frozen cadavers.

These observations are essential in the roentgenologic interpretation of a variety of disease states including defect of the mesocolon with internal herniation into the lesser sac, masses developing within the mesocolic leaves, secondary effects on the descending duodenum from carcinoma of the hepatic flexure, extension of neoplasms of the duodenum to involve the colon, acute pancreatitis, abdominal aneurysm, and distinction of an abscess of Morison's pouch from an inframesocolic abscess.

Diagnosis of spread from colonic carcinoma by the effect of lymph node metastases upon the duodenojejunal junction is shown.

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SIGNIFICANCE OF ILEUS IN PERFORATED VISCUS*

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ONE of the few truly pathognomonic roentgenographic signs is the demonstration of free air in the peritoneal cavity following perforation of a hollow abdominal viscus. On the average, pneumoperitoneum can be demonstrated in approximately 80 per cent of such cases. Various series have reported the incidence of demonstrable pneumoperitoneum at anywhere from 70 per cent to as high as 90 per cent, the range depending on the aggressiveness with which the examination is pursued.[2] In addition to the usual technique of upright and supine or decubitus roentgenograms of the abdomen, together with roentgenograms of the chest to demonstrate free air under the diaphragm, various additional techniques have been used including positioning of the patient in such a way as to attempt demonstration of an ulcer niche in either the stomach or duodenum by entrapped air, or even by the use of water soluble contrast media to determine the actual escape of gastrointestinal contents through the perforation.[2]

Because of the well known diagnostic certainty of free air demonstration, the absence of free air in about 20 per cent of patients who have a perforation often leads to delay in therapy management. This may be the case even in those patients who have fairly characteristic or highly suggestive clinical findings. We noted that although these patients had symptoms of severe abdominal pain, there was almost never roentgenographic evidence of small bowel distention, even when there was obvious perforation. By reviewing all consecutive cases of ruptured hollow viscus seen in our hospital, we came to the conclusion that the presence or absence of ileus was an extremely important finding as an additional roentgenographic sign to confirm a clinical suspicion in the absence of demonstrable free air and also as an accurate guide to the operating surgeon about possible complications.

MATERIAL AND METHOD

We have reviewed 58 consecutive cases of perforated hollow abdominal viscus observed over a 3 year period. These cases were examined with an upright chest roentgenogram to give optimal demonstration of the leaves of the diaphragm, together with supine and upright roentgenograms of the abdomen. More aggressive techniques were not employed. For the purposes of this study, all films were reviewed to evaluate the presence or absence of pneumoperitoneum and the presence or absence of ileus. In all cases a diagnosis was established by surgical exploration.

RESULTS

The results are summarized in Tables I, II, III and IV. Significant points to be noted are that 48 of the 58 patients in the series demonstrated a pneumoperitoneum, with an incidence of 83 per cent, indicating that our demonstration of free air corresponds well to the frequency of demonstration by others. It should also be noted that the 10 patients with no free air showed no evi-

TABLE I

CAUSE OF PERFORATION

	No. of Cases
Perforated duodenal ulcer	52
Bowel obstruction with perforation (strangulated hernia)	1
Carcinoma of colon with perforation	1
Sigmoid diverticulitis with perforation	1
Volvulus of the cecum with perforation	1
Sigmoid ulcer with perforation	1

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
From the Department of Radiology, St. Joseph Mercy Hospital, Pontiac, Michigan.

TABLE II

PRESENCE OR ABSENCE OF PNEUMOPERITONEUM

No. of patients	58	
Pneumoperitoneum	Ileus	No Ileus
48 (83 per cent)	8	40
No pneumoperitoneum		
10 (17 per cent)	0	10

dence of ileus. Of the 48 patients who presented with free air, 8 of these demonstrated ileus of varying degrees in addition to the free air. These 8 patients had either peritonitis as a complication of perforated duodenal ulcer or another intestinal source of free air. Fifty-two of the 58 patients were found to have a perforated duodenal ulcer at the time of surgery. Fifty of these were uncomplicated, but 2 had advanced peritonitis. The 2 who had complications presented with free air and ileus, while the remaining 50 mostly showed free air with some having no free air, but none showed ileus. Of the 6 additional patients who presented with ileus, the perforations were found to be on the basis of bowel obstruction due to inguinal hernia with perforation, carcinoma of the colon with obstruction and perforation, perforated sigmoid diverticulitis, volvulus of the cecum with perforation, and perforation of a stercoral ulcer of the sigmoid. It should be also noted that there was no correlation between the duration of symptoms and the presence or absence of complications.

REPORT OF CASES

CASE I. (Fig. 1, *A* and *B*). A 31 year old male with a past history of duodenal ulcer suffered severe abdominal pains. He came to the hospital 16 hours later, at which time roentgenograms showed free air under the diaphragm with no other findings. At surgery a perforated duodenal ulcer was plicated. There was no evidence of peritonitis. Recovery was uneventful.

Comment. This is a typical case of uncomplicated duodenal ulcer perforation. Although 16 hours had elapsed, there was no ileus.

CASE II. (Fig. 2, *A* and *B*). A 59 year old female was admitted following 10 days of abdominal pain, loss of appetite and progressive weakness. On admission she was obviously very ill with a temperature of 102.4° F., cough, and a blood pressure of 90/60. Chest roentgenograms showed pneumonia. Roentgenograms of the abdomen showed free air but no ileus. Gastrografin studies clearly demonstrated a perforated ulcer. At surgery the ulcer was plicated. There was no evidence of peritonitis. Recovery was uneventful.

Comment. Case II demonstrates an example of perforation which had been present for over a week and showed only free air. In the absence of peritonitis, there was no ileus. The very long time interval was of no significance

CASE III. (Fig. 3, *A* and *B*). A 78 year old female with a known duodenal ulcer and with previous episodes of gastrointestinal bleeding was admitted for question of recurrent bleeding. During hospitalization severe pain and distention developed. Roentgenograms showed massive pneumoperitoneum and marked ileus.

At surgery, duodenal scarring without perforation was found. The source of the pneumoperitoneum was determined to be a perforated stercoral ulcer of the sigmoid without peritonitis.

Comment. Case III is an example of perforation in areas of the gastrointestinal tract other than the duodenum. The different character of the intestinal contents might account for the rapid development of ileus.

CASE IV. (Fig. 4, *A* and *B*). A 69 year old female with a previous history of duodenal ulcer

TABLE III

COMPLICATIONS

	No. of Cases	Ileus	No Ileus
Uncomplicated ulcer perforation	50	0	50
Ulcer perforation with peritonitis	2	2	0
Perforation of other areas	6	6	0

TABLE IV

PRESENCE OR ABSENCE OF FREE AIR

	Free Air	No Free Air
Perforated duodenal ulcer	42	10

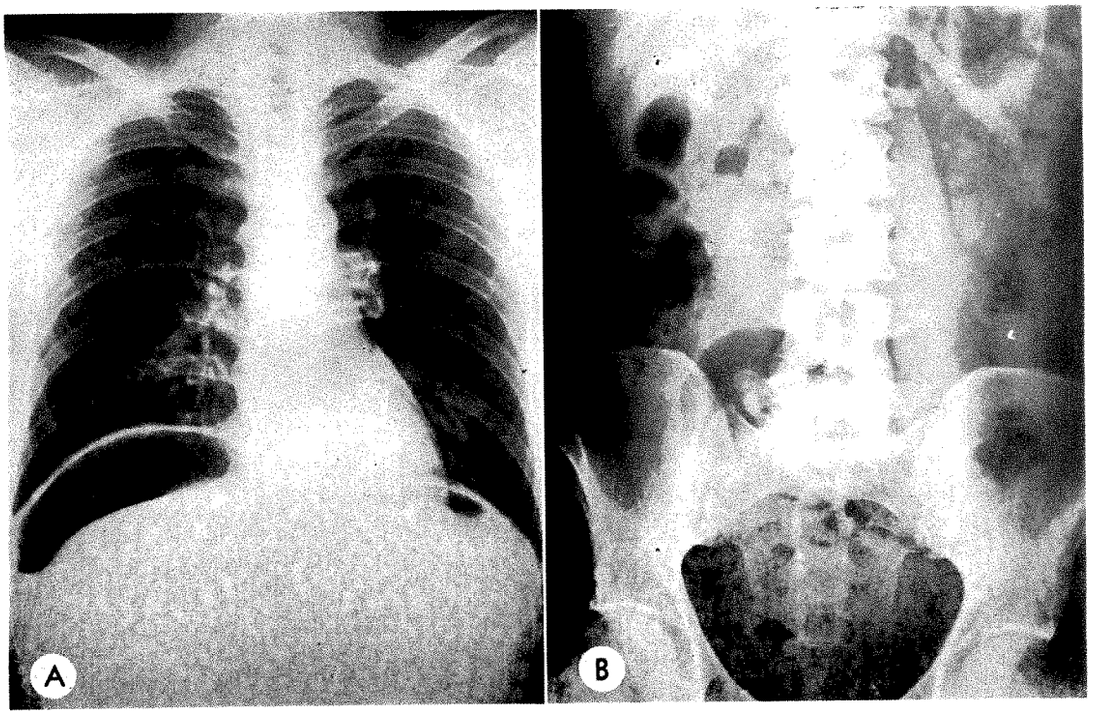


FIG. 1. Case I. (*A* and *B*) Obvious pneumoperitoneum. No abnormalities of bowel gas appearance. Uncomplicated perforated duodenal ulcer.

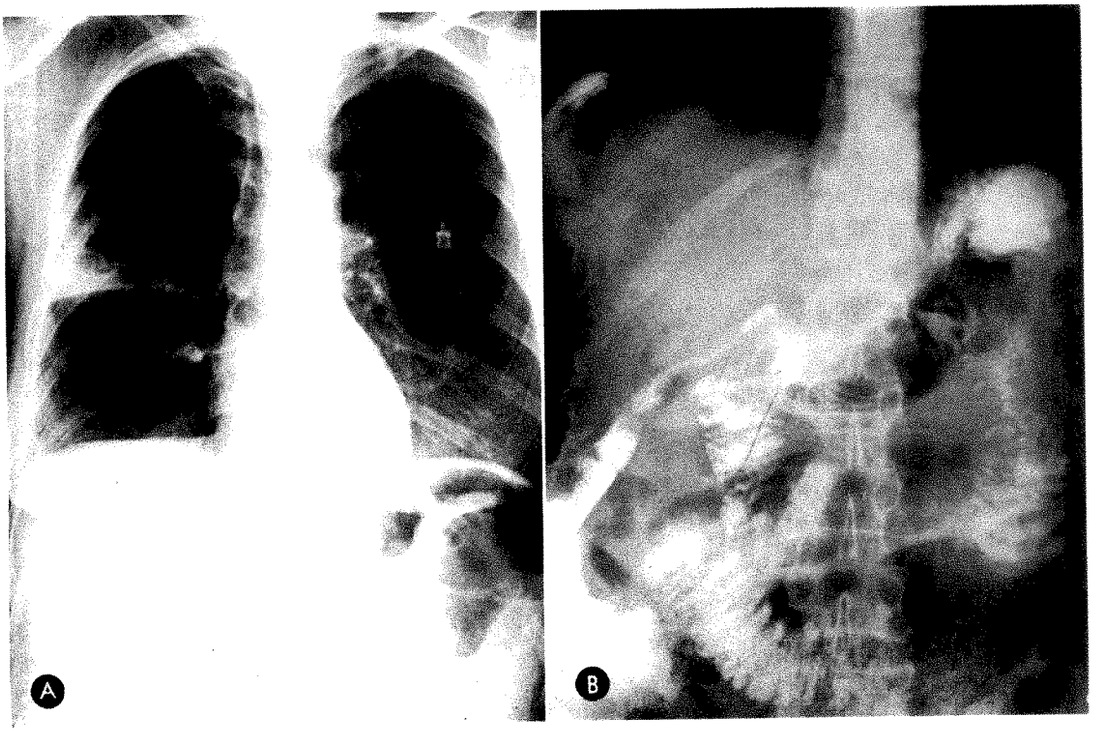


FIG. 2. Case II. (*A* and *B*) Incidental pneumonia, but no pneumoperitoneum or ileus. Gastrografin study demonstrates perforation.

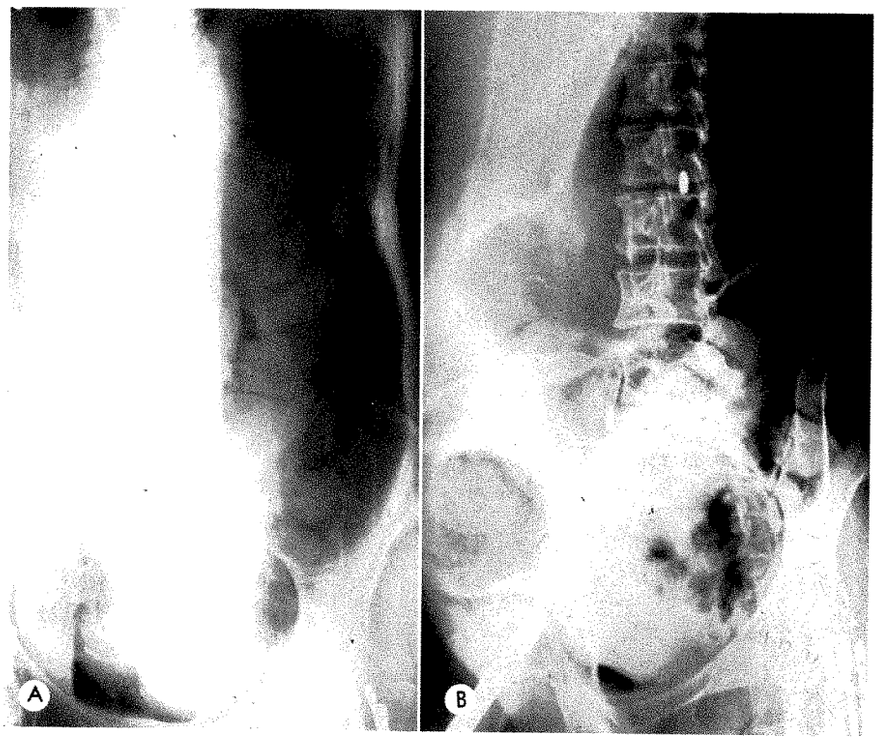


FIG. 3. Case III. (*A* and *B*) Massive pneumoperitoneum and ileus secondary to perforation of colon.

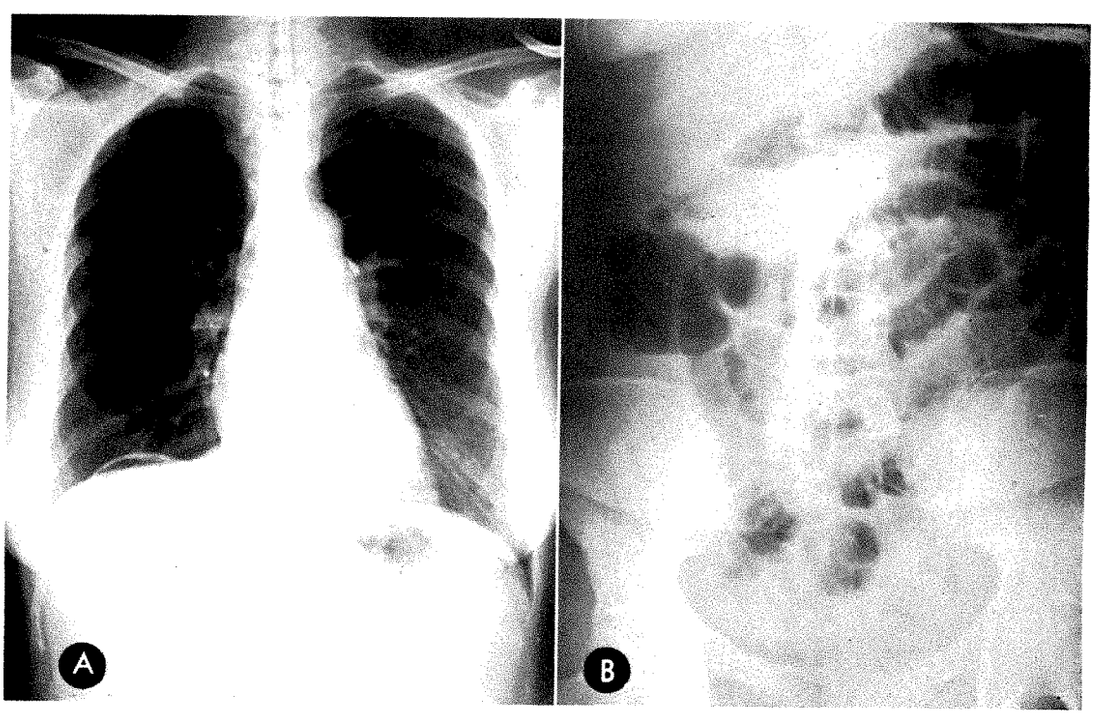


FIG. 4. Case IV. (*A* and *B*) Pneumoperitoneum following perforated duodenal ulcer with peritonitis. Ileus is present as indication of complication.

came to the hospital 12 hours after the onset of severe abdominal pain. Roentgenograms showed free air under the diaphragm and marked ileus. At surgery, a ruptured duodenal ulcer and generalized peritonitis were found.

Comment. Case IV is an example of a perforated duodenum with peritonitis as a complication and ileus. It is interesting to note that the time interval was rather short.

Case V. (Fig. 5). A 32 year old patient with severe abdominal pain came to the Emergency Room. There was a previous history of abdominal pain relieved by antacids, but no proven duodenal ulcer. Roentgenograms were normal with no evidence of free air or ileus. Because of the overwhelming clinical evidence suggesting a ruptured duodenal ulcer, exploration of the abdomen was done. An uncomplicated ruptured duodenal ulcer was found and repaired.

Comment. This case illustrates the problem of diagnosing a ruptured ulcer in the absence of free air. The absence of ileus in such cases favors the probability of ulcer rupture.

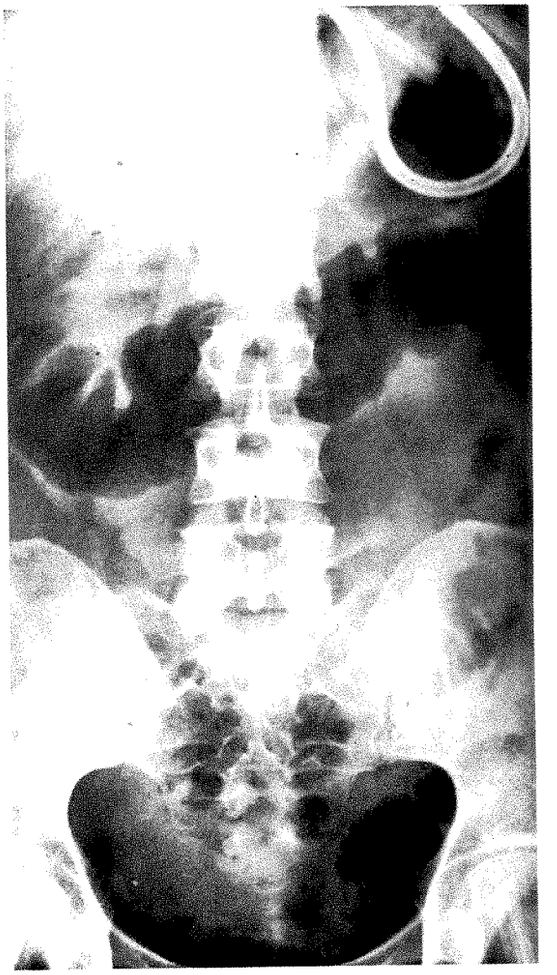


Fig. 5. Case V. Normal study with neither ileus nor pneumoperitoneum. Classical clinical picture suggested uncomplicated perforation of duodenal ulcer.

DISCUSSION

We feel that this review leads to valid conclusions for evaluating abdominal roentgenograms on a patient with highly suspicious clinical signs of a perforated viscus. It is obvious that the best and most significant finding to diagnose a ruptured hollow viscus is the presence of free air.[1] If there is only free air present, with no small bowel findings, the source of the perforation should arise from a perforated duodenum. If the clinical findings are highly suggestive and there is no evidence of free air, the absence of ileus provides supporting evidence that a ruptured duodenal ulcer may indeed be present in spite of the absence of the best known sign. The determination of the next step here might be to proceed directly to surgical repair or try more aggressive diagnostic techniques, including the use of small amounts of water soluble contrast material.[4] On the other hand, if free air is found and there is evidence of ileus, one should be alerted to the probability that the perforation of the duodenum is accompanied by peritonitis or that the source of the air is from some other hollow viscus within the abdomen.

The physiologic basis for the small bowel reaction is not completely clear. Frimann-Dahl, commenting on the absence of ileus in perforated viscus, expressed the opinion that most of these patients are seen early after the onset of symptoms for roentgenographic examination and that nearly all of them have hyperacidity because of their ulcer disease. He felt that the first bowel reaction was a chemical peritonitis which takes some time to recede before a bac-

terial peritonitis can develop. He felt it was not until there was bacterial peritonitis present that conditions were established for extensive paralysis and distention of the bowel.[3] The difference in intestinal flora should provide a ready explanation for the rapid development of peritonitis following perforation of the colon. This would explain the differences in roentgenologic findings. Somewhat similar observations were made by Ling in evaluating the abdominal findings in intussusception in children.[5] It is interesting to note that in his series involving a different disease entity, the presence of small bowel distention was also a more significant measure of the severity of the disease and its complications than was the time element involved.

SUMMARY AND CONCLUSIONS

1. Fifty-eight cases of ruptured viscus are reviewed and analyzed for the presence of free air and small bowel ileus.

2. Eighty-three per cent of these cases showed evidence of free air.

3. The findings would indicate that the presence of free air in the absence of ileus is almost always on the basis of a ruptured duodenal ulcer. The absence of free air and the absence of ileus with good clinical findings should increase the probability of a ruptured ulcer. The presence of free air with ileus indicates that the source of perforation is usually not a ruptured duodenal ulcer, but some other abdominal hollow viscus. If the source of perforation is a duodenal ulcer, the presence of ileus indicates a complication of the perforation.

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LYMPHOSARCOMA OF THE COLON*

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LYMPHOSARCOMA of the colon is a distinctly uncommon entity whether representing a site of primary involvement or a manifestation of a diffuse systemic disorder. Despite its rarity, there are certain roentgenographic features which should suggest the diagnosis to the radiologist. The diffuse, polypoid presentation of colonic lymphosarcoma has been the subject of previous reports.[3,5] However, less well appreciated are the patterns of lymphosarcoma in the adult that produce roentgenographic changes simulating other, more common diseases of the colon.

It is the purpose of this report to illustrate and describe the various modes of lymphosarcoma of the colon as demonstrated by barium enema examination.

BACKGROUND

By 1960 more than 500 malignant lymphomas of the large and small intestine had been reported. Although systemic lymphoma is a common disease entity, colonic involvement is rare.[1] Rosenberg *et al.*[4] were able to collect 1,269 cases of lymphoma of all histologic varieties and reported colonic involvement in only 84. Probably less than 0.5 per cent of all colonic malignancies are lymphosarcomas.

Glick and Soule[2] were able to cite 38 cases of primary colonic lymphomas in the world literature and contributed 27 additional cases from their experience at the Mayo Clinic up to 1966. Subsequently, Wychulis *et al.*[6] reported 69 cases of lymphoma of the colon from the same institution, covering a period of 57 years. They concluded that the roentgenographic features of primary and secondary lymphomas were indistinguishable. Barium enema examination demonstrated a lesion in 90 per cent of their cases.

The gross pathologic appearance of lymphosarcoma is dictated by which layers of the bowel wall are diseased. The lamina propria layer, that portion of the mucous membrane just below the epithelium, contains scattered lymphatic tissue. Disease in this region produces a mucosal pattern of lymphosarcoma. Lymphatic nodules are also present deep in the submucosa and may extend into the serosal layers as well. Finally, large mesenteric masses are frequent findings in this entity.

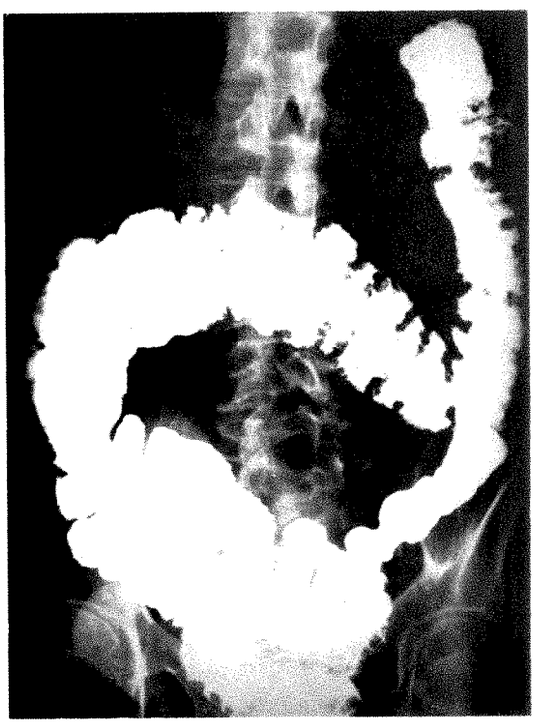


FIG. 1. The barium filled colon presents a "soapsuds" appearance. Also, note the mucosal irregularity at the inferior margin of the transverse colon.

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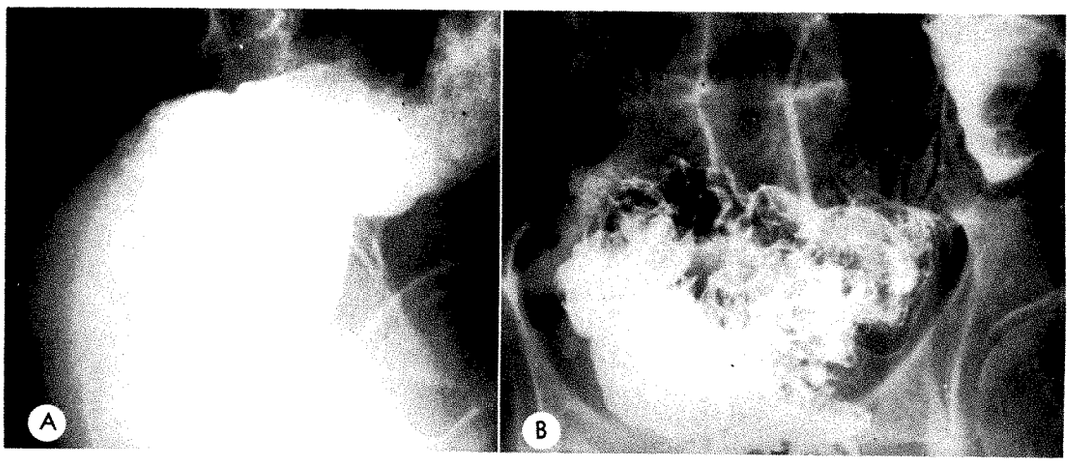


FIG. 2. (*A* and *B*) Barium and air contrast study of the rectosigmoid colon shows numerous polypoid lesions with frank mucosal infiltration.

Lymphosarcoma of the colon is twice as common in men as in women. Its clinical presentation is usually nonspecific with abdominal pain, weight loss, mass or bleeding as the principal features. Intussusception, producing signs and symptoms of colon obstruction, is an uncommon feature in adult lymphosarcoma. Chronic ulcerative colitis has been described as a predisposing condition in several adult patients.

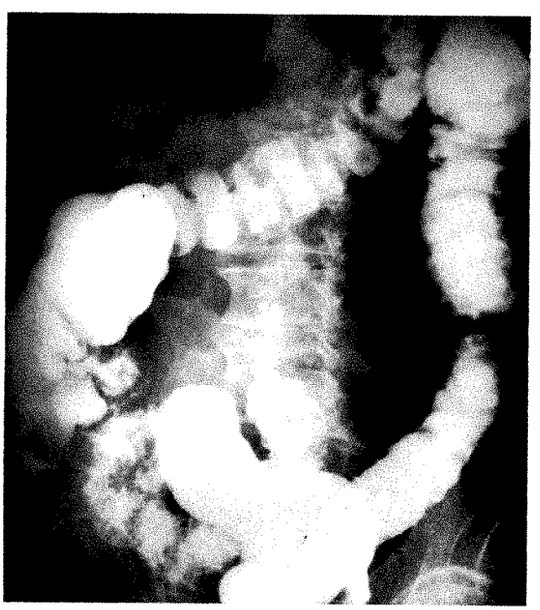


FIG. 3. Simultaneous ileal and colonic lymphosarcoma is observed at the barium enema examination. (Courtesy of Dr. Alexander Belman.)

ROENTGENOGRAPHIC FINDINGS

The distinctive roentgenographic patterns of colonic lymphosarcoma reflect the

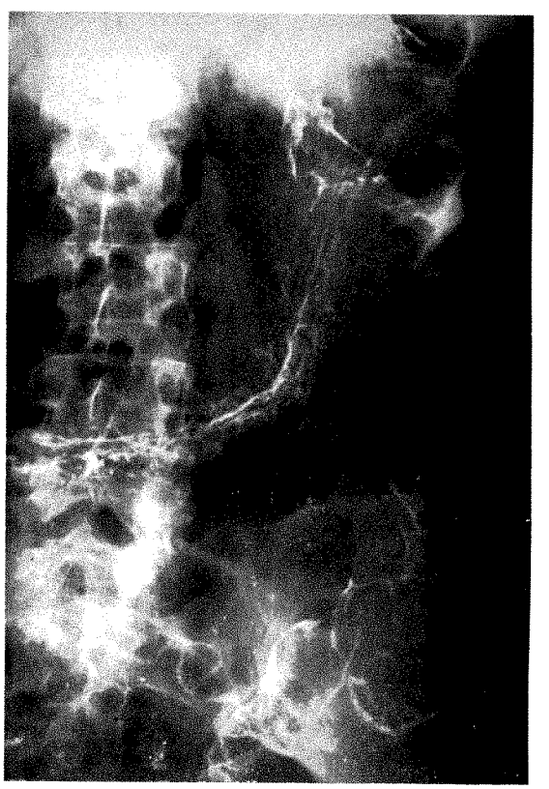


FIG. 4. A bulky mass is seen to extend over a long segment of the colon. A large ulcer is shown at the proximal extent of the lesion. (Courtesy of Dr. Leonard Barris.)



Fig. 5. A nonuniform infiltrating lesion, primarily submucosal, is observed through a long segment of the colon.

various sites of lymphosarcomatous change within the colonic wall. Mucosal disease manifests itself in a variety of forms. Diffuse, nodular mucosal involvement presents a rather characteristic "soap-suds" appearance when the colon is opacified with barium (Fig. 1). The colon is seen to distend well with air and, in fact, may remain distended on postevacuation roentgenograms.

Differentiation of this entity from the true polyposis syndromes or the pseudopolyps of ulcerative colitis may prove difficult. An unusual flaccidity and lack of shortening of the colon are helpful findings in distinguishing between pseudopolyposis and other polyposis states, including lymphosarcoma. However, it is the presence of mucosal irregularity which separates lymphosarcoma from the true polyposis states, since bowel wall infiltration would be most atypical in the latter without obvious superimposed malignancy (Fig. 2, *A* and *B*; and 1). If there are associated nodular lesions in the small bowel, especially in the



Fig. 6. (*A* and *B*) Localized "thumbprinting" and haustral thickening are seen at the level of the ileocecal valve. Air contrast study confirms the rigidity of this part of the colon.

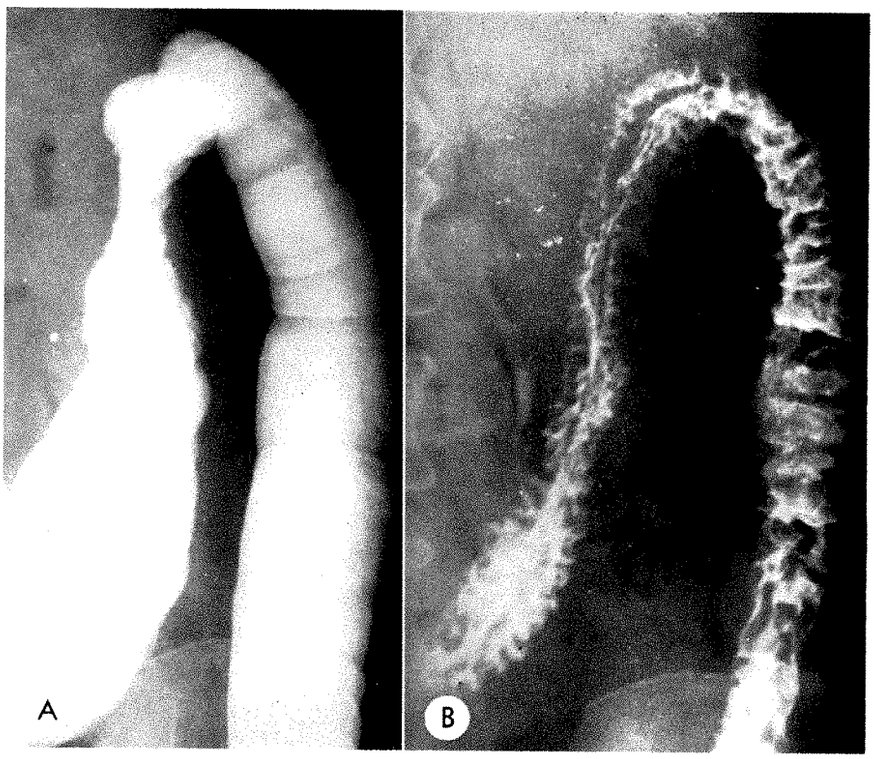


FIG. 7. (*A* and *B*) A stricture is seen at the distal transverse colon. Postevacuation roentgenogram shows a slight mass effect without mucosal alteration. (Courtesy of Dr. Bernard Epstein.)

ileum, the diagnosis of lymphosarcoma is almost certain (Fig. 3).

Solitary polypoid masses were not observed in this group of patients. However, bulky, irregular masses extending over a long segment of colon, and associated with angular, often large ulcerations, present a roentgenographic picture of a neoplastic process in keeping with the diagnosis of lymphosarcoma (Fig. 4). This is the pattern which is commonly seen in the stomach and small bowel.

Submucosal nodules or "thumbprints" are the hallmark of several types of colonic diseases. Intramural hemorrhage and granulomatous inflammatory disease are the most common entities causing such defects through a long segment of colon. The "thumbprinting" of intramural hemorrhage and edema, whether secondary to arterial ischemia or a bleeding diathesis, is relatively uniform in its size and configuration. In contrast, the submucosal form of colonic lymphosarcoma produces more structural alteration in the bowel wall, resulting in a more disorganized pattern (Fig. 5). In addition, haustral markings remain rigid and thickened—another finding consistent with submucosal disease (Fig. 6, *A* and *B*). Skip areas and fistulae are not features of large bowel lymphosarcoma.

When the colonic wall is involved in a "plaque-like" fashion, a circumferential narrowing of the bowel lumen is observed. In this form there is surprisingly little exophytic mass. The mucosa is seen to remain intact on the postevacuation roentgeno-

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FIG. 9. (*A* and *B*) Colonic obstruction on plain film roentgenogram is secondary to an annular constricting lesion in the descending colon.

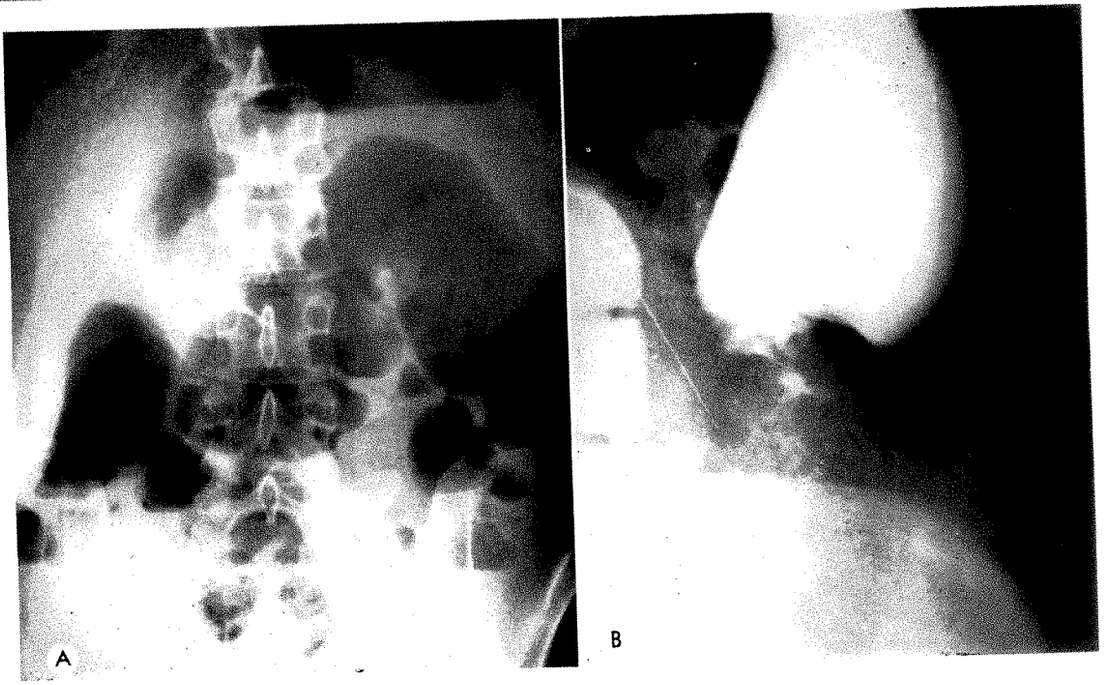


FIG. 8. A localized extrinsic defect is seen in the mid-descending colon along with numerous diverticula.

grams (Fig. 7, *A* and *B*). This roentgenographic pattern of lymphosarcoma must be considered in the differential diagnosis of stricture type lesions of the large bowel, perhaps being more typical of postischemic or postinflammatory disease with mucosal healing or scirrhus carcinoma.

Subserosal lymphosarcoma is virtually impossible to differentiate from serosal implants associated more commonly with a metastatic malignancy. Well-defined obtuse angles are observed at the edges of the mass (Fig. 8). Careful attention to mucosal detail shows the lack of transmural involvement. Diverticulitis with localized abscess formation is also a consideration in these cases, especially when diverticulosis is an accompanying feature.

The annular constricting lesion characteristic of adenocarcinoma of the colon is a rare manifestation of lymphosarcoma. However, other lymphomatous processes,



especially reticulum cell sarcoma, produce this appearance not infrequently and may result in colon obstruction (Fig. 9, *A* and *B*).

SUMMARY

Lymphosarcoma of the colon is an uncommon disease entity. The roentgenographic findings which have been most helpful in differentiating lymphosarcoma from other colonic disorders include the presence of: diffuse nodular lesions with irregular margins, the latter suggesting infiltration of the bowel wall; bulky ulcerating masses extending over a long segment of the colon; an association of nonuniform submucosal nodules and marked haustral thickening and circumferential narrowing of the colonic lumen with intact mucosa.

Finally, any colonic lesion in a patient with known systemic lymphoma is suspect for being lymphosarcoma of the colon.

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ANGIOGRAPHIC FINDINGS IN VILLOUS TUMORS OF THE COLON*

By PEDRO OLAFSSON RIBA *and* ANDERS LUNDERQUIST
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IN the last 10–15 years increasing interest has been devoted to the villous tumors of the colon, and many reports on their incidence, distribution, clinical findings, pathologic-histologic features and roentgenologic pattern on barium studies have been published.[2–6,8] A review of the radiologic literature, however, has so far failed to show any single case of villous tumor demonstrated angiographically. Therefore, it was thought advisable to report 1 case of solitary villous tumor of the rectum and another case of villous tumor occurring together with a malignant lesion in the ascending colon, to describe the angiographic findings, to correlate their pattern with the roentgenologic data given by conventional barium enema examination and with the histo-pathologic picture, and to discuss the value of the angiographic examination from a differential diagnostic point of view.

The appearances of a typical villous tumor on routine barium enema examination are quite characteristic, and have been amply described,[4,5,8] almost allowing for spot diagnosis. The lesion reveals itself as a broad-based, poorly demarcated polypoid mass with the barium fluid insinuating as thin linear streaks between the folds and villi of the tumor, giving its surface a typical feathery pattern best seen on the postevacuation roentgenogram and on double contrast barium enema roentgenograms. No ulceration or signs of infiltration are seen, and the tumor-bearing part of the colonic wall shows some degree of variability in shape with filling and emptying. Tumors with classic patterns are mostly located in the rectosigmoid,[1,8] their villous surface turning more polypoid and presenting as polypoid filling defects, the more proximal in the colon the tumor lies.[5] The occurrence of malignant lesions in association with a villous tumor is reported in as high as about one-quarter of patients.[5,6]

The villous tumor of the colon is a potentially malignant lesion, and values of malignancy on serial section in clinically benign villous tumors ranging between 20–69 per cent have been given.[5,6,8] Difficulty to demonstrate a malignant villous tumor on biopsy has been stressed, with a false negative diagnosis in up to 23 per cent of the cases.[7] Serial sections through the tumor are imperative for the accurate evaluation. The presence of invasive cancer in a villous tumor cannot be excluded by the gross appearance, rectal palpation or sigmoidoscopic examination, nor by conventional roentgen procedures. Some criteria for differentiating benign and malignant tumor have been put forward. Persistent narrowing of part of the bowel lumen, ulceration, and a rigid irregular contour are signs pointing to possible malignancy. Some authors, however,[5,6] find the size of the lesion the only reliable criterion: the larger the lesion, the higher the incidence of malignancy. Small tumors are said to have a higher percentage of malignancy, when situated above the peritoneal reflection, with a greater tendency to metastasize to regional lymph nodes and the liver.[6,8]

The clinical symptoms and signs are fully known, ranging from vague abdominal discomfort with more or less loose mucus stools with or without rectal bleeding, to profuse discharge of large amounts of mucus and great fluid loss leading to bizarre examples of electrolytic imbalance.[3]

* From the Department of Diagnostic Radiology (Director: Prof. Olle Olsson), University Hospital, Lund, Sweden.
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A small percentage of patients are symptom-free and quite a few tumors are found incidentally.

The histologic appearance of the villous tumor will not be discussed in this communication.

REPORT OF CASES

CASE 1. A 64 year old male was admitted to the hospital because of vague abdominal discomfort for several years, not very marked until 5–6 months prior to admittance. The patient had noticed the passage of thin, narrow stools and mucus, but denied diarrhea, bleeding, pain or weight loss. The past history revealed nothing of interest.

Physical examination was unremarkable and laboratory studies were within normal boundaries.

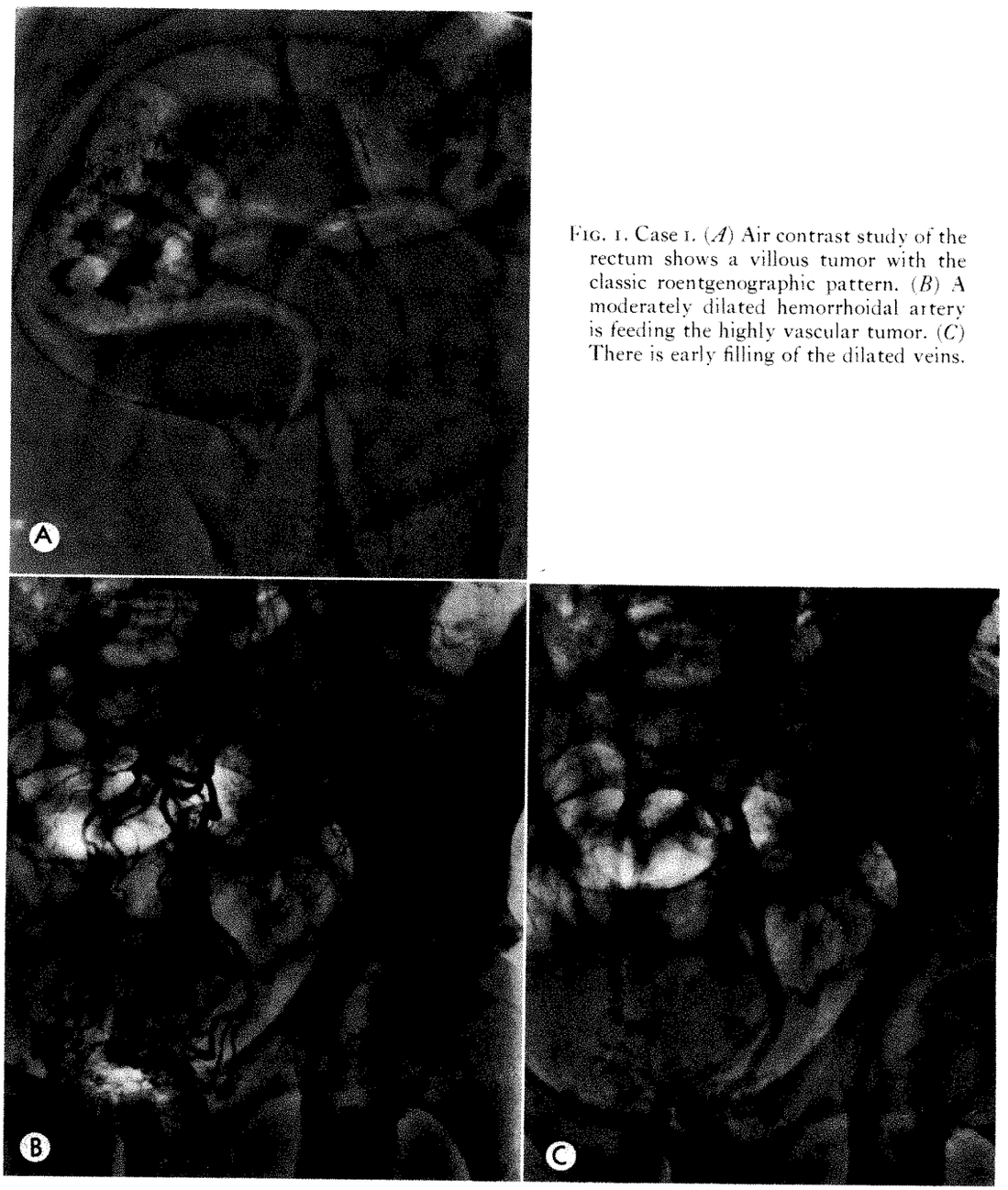


FIG. 1. Case 1. (*A*) Air contrast study of the rectum shows a villous tumor with the classic roentgenographic pattern. (*B*) A moderately dilated hemorrhoidal artery is feeding the highly vascular tumor. (*C*) There is early filling of the dilated veins.

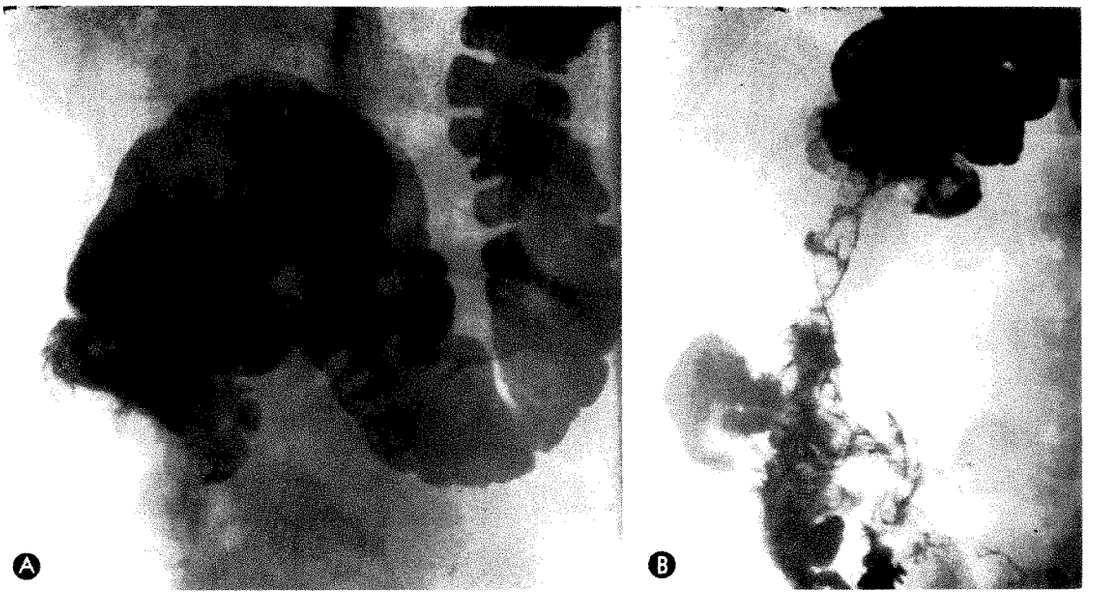


Fig. 2. Case II. (*A*) There is obstruction to the passage of the contrast medium in the ascending colon on barium enema examination. (*B*) Small bowel roentgenogram reveals a stricture in the ascending colon.

Roentgen examination of the colon showed a large broad-based polypous tumor in the posterior wall of the rectum. The tumor had a very irregular surface, with the barium extending into the tumor in linear streaks giving the lesion the characteristic feathery pattern of a villous tumor, and was demonstrated on double contrast examination (Fig. 1*A*). No signs of ulceration were seen, and the wall of the rectum showed no evidence of infiltration.

Angiography of the inferior mesenteric artery revealed a dilated superior hemorrhoidal artery feeding the richly vascularized tumor which was intensely stained in the capillary phase. The smaller arteries in the center of the tumor were slightly irregular, but no tumor vessels were seen. The draining hemorrhoidal veins were greatly dilated and filled earlier than the veins from the sigmoid (Fig. 1, *B* and *C*).

Two out of 3 rectal examinations, including sigmoidoscopy, failed to disclose the extremely soft, pale and yielding tumor located about 4 cm. high in the rectum. Incisional biopsy showed the characteristics of a villous tumor without signs of malignancy.

At surgery a villous mass, soft and pliable, about 5 cm. in diameter, was found in the posterior wall of the rectum. An abdominoperineal resection was performed with an uneventful postoperative course.

The pathologic report was that of a villous adenoma with primarily exophytic growth, a moderate degree of atypia without signs of extension of the tumor beneath the muscularis mucosae or evidence of malignant transformation.

The patient, now 6 years after the operation, is doing well with no signs of recurrence of the tumor.

Case II. A 53 year old male had complained of tiredness with some ill-defined pain in the abdomen and weight loss for 2 months. Laboratory examination disclosed severe anemia. The patient denied anorexia; he had no blood or mucus in the stools and no constipation.

Roentgen examination of the colon showed a filling defect in the proximal part of the ascending colon, just beneath the hepatic flexure, with obstruction to the passage of the contrast medium. The filling defect had a slightly polypous upper boundary. After a barium meal a large stricture was seen in the lower segment of the ascending colon. Other parts of the colon were difficult to interpret because of large quantities of fecal contents (Fig. 2, *A* and *B*).

Angiography of the superior mesenteric artery showed 2 different tumors in the ascending colon. The more distal tumor, close to the hepatic flexure, was highly vascular with distinct contrast stain in the capillary phase and

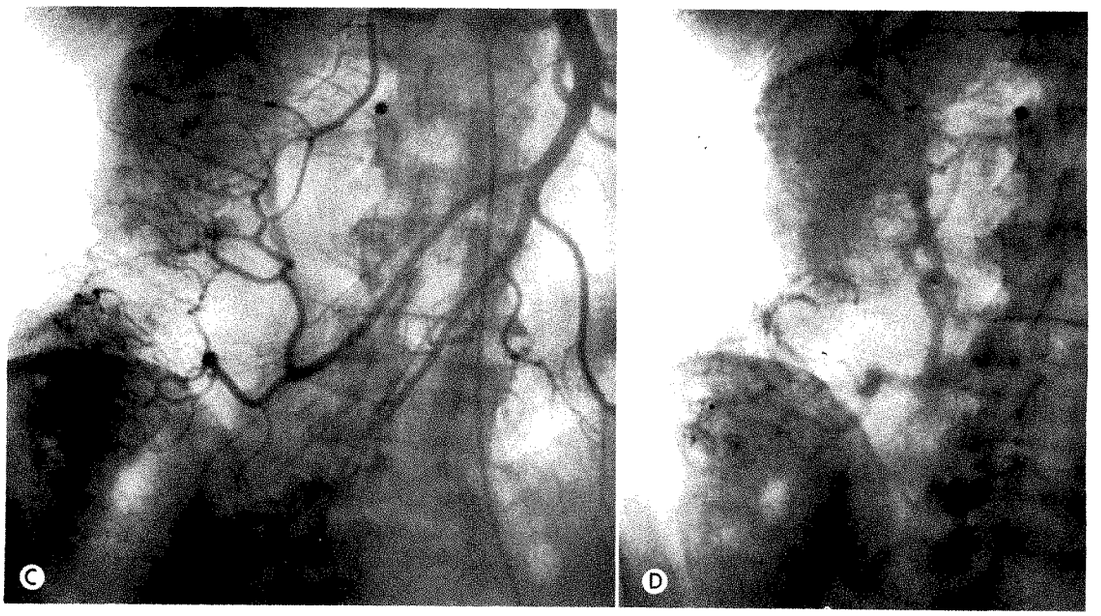


FIG. 2. (*C*) Superior mesenteric angiography. Arterial phase. Irregular, dilated arteries are visible in the carcinoma of the lower part of the ascending colon. There are slightly dilated and tortuous arteries in the villous tumor in the upper part of the ascending colon. (*D*) Venous phase. Irregular, dilated veins are seen in the carcinoma. There is dense accumulation of the contrast medium in the villous tumor and a small number of slightly irregular veins.

early filling of the mesenteric veins. Although some arteries and veins were slightly irregular, no tumor vessels could be seen. The more proximal lesion showed fewer, but much more irregular arteries with early filling of the draining veins, but no contrast accumulation in the capillary phase (Fig. 2, *C* and *D*).

No attempt of differential diagnosis was made from the angiography at the time of examination and the lesion as a whole was labelled as an adenocarcinoma of the colon. Celiacography showed ill-defined arterial changes compatible with metastases of the liver.

Surgical exploration revealed a tumorous lesion about 6 cm. in diameter in the ascending part of the colon with a smaller tumor a little more distal, close to the hepatic flexure. Metastases were palpated in the liver. Colectomy and ileo-rectostomy were performed.

The surgical specimen disclosed a cauliflower-like, 4–5 cm. large polypous tumor in the upper part of the ascending colon. Four to 5 cm. below this was another broad-based tumor about 5 cm. in diameter with a slightly polypous surface. In the transverse and descending colon, multiple polyps up to the size of a walnut were found. Furthermore, a 2×2 cm. polypous tumor and a 3×2 cm. large tumor infiltration were disclosed in the sigmoid.

The final pathologic report of the uppermost tumor in the ascending colon was a noninfiltrating villous tumor with moderate cell atypia. The lower tumor was an adenocarcinoma partly infiltrating all layers of the wall of the bowel. The polyps in the transverse and descending colon were all benign. The smaller polyp in the sigmoid showed evidence of malignant transformation and the larger tumor proved to be an adenocarcinoma extending to, but not penetrating, the muscularis mucosae.

DISCUSSION

As already stated, the gross appearance of a villous tumor may be quite variable. As a general rule, tumors lying in the lower part of the colon have a more villous pattern, whereas tumors located more proximally in the right colon are more polypoid. Exceptions to the rule are, however, common, as pointed out by several authors.[5] Our reported villous tumors were located on opposite extremes in the colon, the rectal lesion showing all the charac-

teristics of a typical villous tumor on conventional barium studies, in full agreement with previously reported cases. Based on size of the lesion one could have expected malignancy. The angiography, however, showed dilated arteries supplying the tumor, but no newly formed tumor vessels were seen. Some of the arteries within the tumor showed small lumen irregularities. In a poorly vascularized adenocarcinoma of the colon this may be the only sign of malignancy at angiography. Hypervascular adenocarcinoma, however, will always show tumor vessels in association with lumen irregularities of the arteries. The lack of tumor vessels in the hypervascular tumor may suggest a way of differentiation. In our Case 1 no traces of malignant transformation could be seen—a fact confirmed by the pathologist's report. The gross appearance of the lesion in the right part of the colon could not be determined from the routine barium examination, neither did angiographic studies give a relevant clue as to the nature of the tumor which was simply labelled as adenocarcinoma. Retrospectively, the angiography, however, revealed clearly 2 different patterns: one tumor was very rich in vessels, some with slight irregularity and intense opacification late in the arterial phase together with early filling of the draining veins; the other tumor was less vascularized and the arteries within the tumor were much more irregular, there was only faint accumulation of the contrast medium in the tumor during the capillary phase, and irregular veins were early filled with contrast medium indicating arteriovenous shunting.

From the point of view of differential diagnosis, 2 other pathologic conditions in the colon can be similarly evaluated by angiography: carcinoid tumors and inflammatory lesions. The carcinoid tumor is also supplied by dilated arteries which show an irregular lumen and distribution within the tumor, and the surrounding small arteries often form a stellate pattern because of shrinking of the tumor, although tumor vessels and arteriovenous shunts have not been demonstrated. In cases of regional enteritis the arteries are likewise dilated, may show lumen irregularities and a typical right angled bifurcation. The veins from the lesion fill early with contrast medium of high concentration.

SUMMARY

Two cases of benign villous tumors of the colon, in which selective mesenteric angiography was performed, are described.

The findings were somewhat different from those reported in other benign and malignant tumors of the bowel.

Information obtained from both conventional barium studies and angiographic examination may suggest the diagnosis.

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COLONOSCOPY AND DOUBLE CONTRAST BARIUM ENEMA EXAMINATION IN CHRONIC ULCERATIVE COLITIS*

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THE barium enema examination is the usual means of assessing the extent and severity of ulcerative disease of the colon. Correlative studies of the roentgenographic and pathologic features carried out on colectomy specimens[2] show that roentgenology often underestimates both the extent and the severity of the disease process. Colonoscopy, with biopsy of the colon, provides a method of studying this problem more systematically. Earlier instruments presented some problems,[3] but with the Olympus CFLB instrument it is usually possible to examine the whole colon.[1]

In the present correlative study, 11 patients, 10 of whom had moderate to severe ulcerative colitis or proctitis of at least 5 years' duration, were examined by double contrast enema and by colonoscopy with biopsy.

MATERIAL AND METHOD

Colonoscopy was carried out using the Olympus CFLB instrument which can be passed to a maximum distance of 185 cm. from the anus.

Eleven patients were examined by colonoscopy, all but 1 of whom had had ulcerative colitis or proctitis of varying severity for at least 5 years. Colonoscopy was undertaken during clinical remission. Preparation for the procedure consisted of a low roughage diet for the previous 5 days, 2 "Senokot" tablets 48 hours and 2 further tablets 24 hours beforehand, and 2 colonic lavages on the morning of colonoscopy.

The premedication was Phenoperidine 2 mg. and Droperidol 10 mg. intravenously for a normal male adult, the dosage being reduced appropriately if indicated. The instrument was passed with the patient in the left lateral position and after the sigmoid colon had been negotiated, the patient was placed in the supine position for the rest of the examination. It was essential to carry out the procedure with roentgen-ray screening facilities available. Occasionally, this helped with the negotiation of acute bends but it also enabled the tip of the instrument to be precisely located for recording purposes, especially during biopsy.

Systematic biopsy specimens of the colon were taken during the examination using flexible biopsy forceps with 2 hemispherical blades each 1.5 mm. in diameter, 2 to 3 biopsy specimens being obtained from each of the ascending, transverse, descending and sigmoid colon. Sometimes it was not possible to biopsy the proximal bowel, because several acute bends in the instrument prevented advancement of the biopsy forceps. Biopsy specimens were also taken from areas of interest such as acute inflammation and polyps. The biopsy specimens, which measured 1–2 mm. in diameter, were postfixed in formal sublimate after initial fixation in 10 per cent formal saline. Following processing and embedding in wax, sections cut at several levels through the biopsy specimen were stained with hematoxylin and eosin.

All patients underwent a barium enema examination within 2 to 3 weeks of the colonoscopy, and during this interval it was ascertained that there was no change in the clinical status. The patients were prepared by instilling 1 liter of warm saline containing 3 gm. of Veripaque into the colon 1

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hour beforehand. This results in colonic emptying and once the patient was comfortable, barium sulphate in warm water (4 parts Micropaque* to 1 part water) was allowed to flow just beyond the splenic flexure. Emptying of the bowel took place through a T-tube connection with the patient still on the table. Air was then injected carefully until the cecum was filled and an extensive series of double contrast films was exposed in the erect, supine and prone positions.

RESULTS

In 3 patients with ulcerative colitis of moderate severity involving the sigmoid and descending colon and the distal transverse colon roentgenologically, visual evidence of involvement of the same extent was obtained and was confirmed by biopsy. These patients are not discussed further.

Three patients with longstanding proctitis but no roentgenologic evidence of more proximal involvement were shown to have normal mucosa visually as far as the proximal transverse colon, but biopsy showed mild inflammatory changes such as slight edema and some increase in cellular infiltrate. In addition, several biopsies showed features indicative of mucosal atrophy consequent upon repeated episodes of colitis, such as reduction in the number of crypts, separation of the crypt bases from the muscularis mucosae and paneth cell metaplasia (Fig. 1). For comparison, a biopsy from a normal descending colon is shown in Figure 2. Another patient with roentgenologic and visual evidence of involvement of the sigmoid colon alone was also shown to have mild histologic changes extending to the transverse colon.

* Damancy & Co. Ltd., Ware, Herts., England.

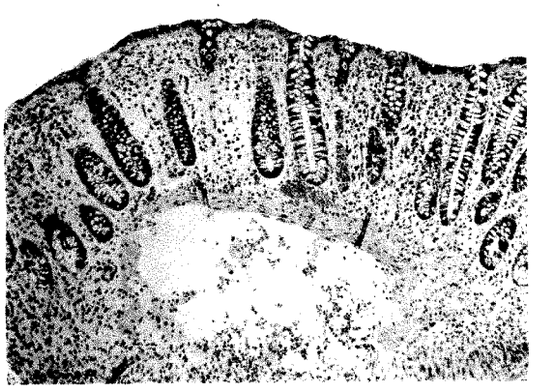


FIG. 1. "Mild" histologic changes in the colon (×90). There is congestion and edema of the lamina propria with a slight increase in the number of polymorphonuclear and plasma cells. There is a reduction in the number of crypts, but the epithelial changes are not marked.

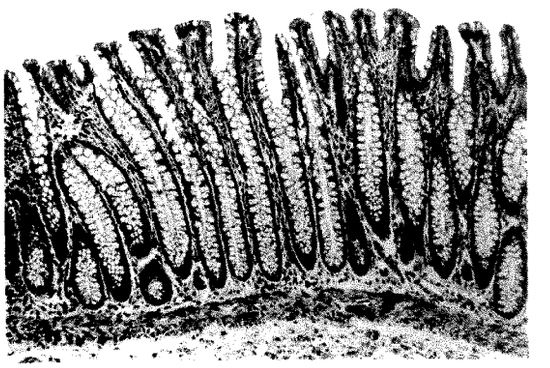


FIG. 2. Biopsy from normal colon (×90). The crypts are regular and parallel with numerous goblet cells and the lamina propria occupies a relatively smaller proportion of the mucosa.

The 4 remaining patients are detailed below. The extent of involvement of the colon in these cases is illustrated diagrammatically in Figure 3.

REPORT OF CASES

PATIENT 1 (male, aged 56 years). This patient developed symptoms 13 years ago, but the diarrhea has been minimal for the past $3\frac{1}{2}$ years.

A double contrast barium enema examination (Fig. 4) showed deformity of the cecum and considerable involvement of the ascending and transverse colon as far as the splenic flexure with loss of haustral pattern and definite mucosal change.

At colonoscopy the instrument was passed to the cecum where the mucosa was seen to be inflamed and edematous. These changes continued to the hepatic flexure but from that point distally the appearances were virtually normal, the only finding being scattered areas

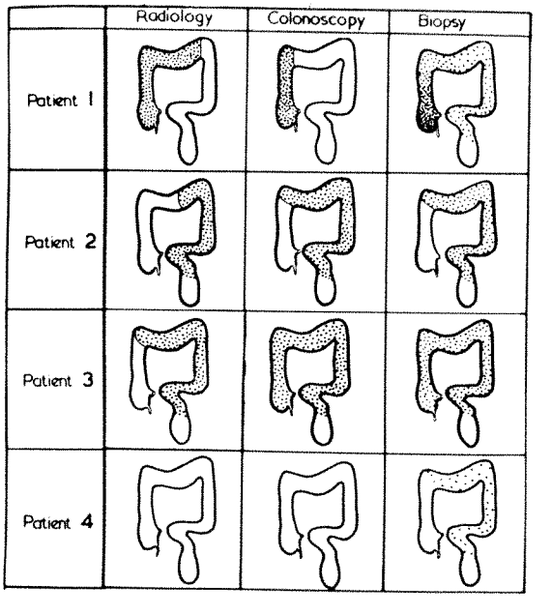


FIG. 3. Extent of colonic inflammation as assessed by roentgenology, colonoscopy and biopsy.

of minimal inflammation. Biopsies showed moderate inflammation in the cecum, ascending, transverse (Fig. 5) and proximal descending colon and mild changes in the distal descending colon.

PATIENT 2 (male, aged 66 years). This patient's first symptoms developed 11 years ago and for the past 4 years they have been low grade with up to 4 soft motions per day and occasional blood and slime.

Barium enema examination showed involvement of the sigmoid and descending colon.

Colonoscopy revealed the mucosa of the cecum and ascending colon to be normal, but the mucosa of the whole of the transverse colon showed numerous areas of slight hemorrhage and exudate and these changes persisted in the descending and sigmoid colon. Biopsy of the ascending colon was not possible, but in other areas the changes were those of chronic ulcerative colitis (Fig. 6).

PATIENT 3 (male, aged 59 years). This patient's symptoms developed 13 years ago and have at times been of considerable severity.

Double contrast barium enema examination showed typical changes of chronic ulcerative colitis extending from the hepatic flexure distally (Fig. 7).

At colonoscopy the cecum and ascending colon were found to be inflamed and inflammation persisted throughout the rest of the colon. At the hepatic flexure there was an area covered by large fleshy pseudopolyps and there was a similar area at the splenic flexure. Multiple biopsies confirmed the presence of chronic ulcerative colitis throughout the colon.

PATIENT 4 (male, aged 43 years). This patient was shown to have proctitis 13 years ago. He responded well to treatment with oral salazopyrine, and topical and systemic steroids, but had an exacerbation 7 years ago and since then has run a chronic course requiring intermittent corticosteroids.

The double contrast barium enema examination was entirely normal.

At colonoscopy, which was carried out as far as the hepatic flexure, no evidence of colitis was found. There were, however, about 40 small polyps in the descending colon, most of which did not exceed 3 mm. in diameter. Mucosal biopsies showed evidence of mild but definite inflammation from the hepatic flexure distally (similar to Fig. 1, but with a more marked inflammatory cell infiltration).

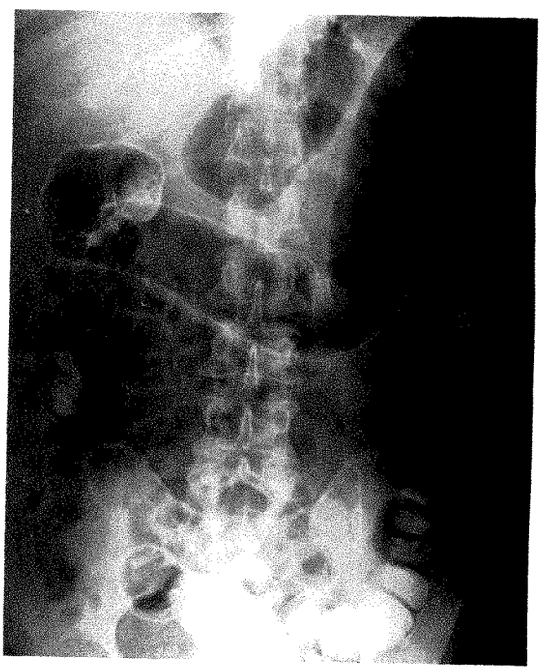


FIG. 4. Patient 1. Deformity of the cecum. Loss of haustral pattern and definite mucosal change in ascending and transverse colon.

DISCUSSION

The recent technique of colonoscopy allows direct examination of the colonic mucosa and also permits biopsy in selected sites of the colon. This has given the opportunity of examining the colon in relatively well patients—particularly those in remission. The procedure is not difficult in patients with chronic ulcerative colitis because shortening of the colon tends to obliterate the normal acute bends, especially in the sigmoid.

The present study demonstrated that roentgenology underestimated the extent and severity of the disease in 8 out of 11 patients. For example, patients thought to have proctitis alone may have biopsy evidence of involvement in the descending colon. In other patients, moderate visual and biopsy changes were present in a roentgenologically normal transverse and ascending colon. In Patient 1 with roentgenologic involvement of the right and transverse colon, biopsy showed a pancolitis. It is thus possible that some cases of "segmental" or right-sided colitis have ulcerative colitis in the whole colon.

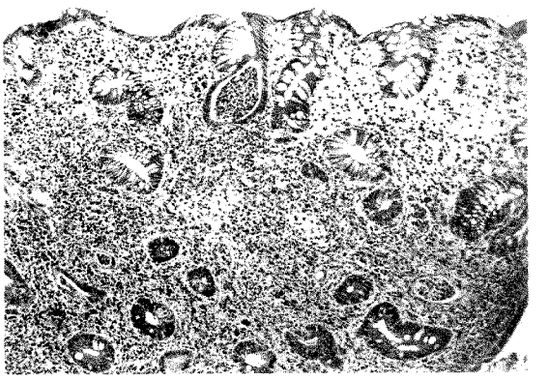


FIG. 6. Biopsy from hepatic flexure (×90). Heavy infiltrate of polymorphonuclear and plasma cells in the lamina propria with crypt abscess formation. Goblet cell depletion and paneth cell metaplasia are observed in the deeper crypts.



FIG. 5. Biopsy from proximal transverse colon (×90). This shows a heavy infiltrate of plasma cells and polymorphonuclear cells with diminution both in the number of crypts and in their goblet cell population.

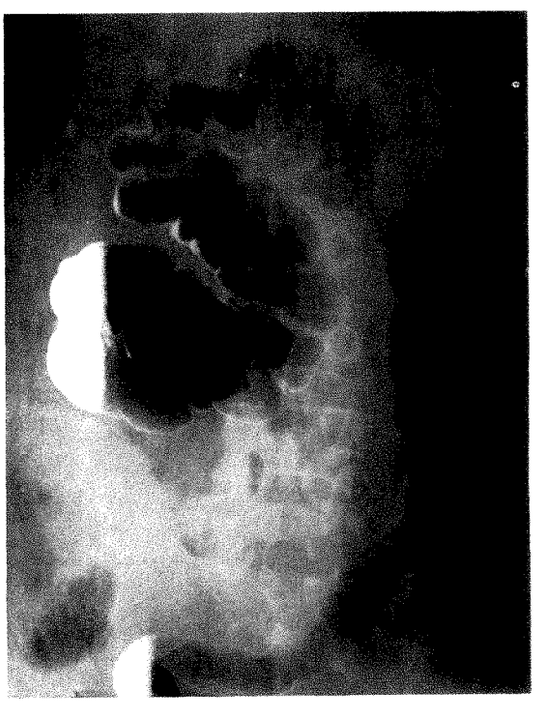


FIG. 7. Patient 3. Extensive changes of ulcerative colitis extending distally from the hepatic flexure.

A study of cases treated by colectomy[2] also demonstrated the limitations of roentgenologic assessment of the colon in ulcerative colitis. Severe mucosal changes tended to be masked by the presence of debris in the colon. On the other hand, roentgenology can demonstrate loss of haustra and the presence of narrowing due to fibrosis which are difficult to assess visually at colonoscopy; for example, the transverse colon in Patient 1 appeared almost normal visually, but both roentgenology and biopsy showed severe involvement. Thus, to some extent, the techniques are complementary.

In the present study, colonoscopy demonstrated other features which were not seen on the roentgenologic study. In Patient 3, pseudopolyps were present in 2 areas and in Patient 4 the descending colon had many tiny polyps. In common with others,[2] we have found that pseudopolyps are more difficult to demonstrate on double contrast studies, compared to conventional enema techniques. Thus colonoscopy can often detect small, localized lesions which may remain undetected by the double contrast enema examination. The ease with which the mucosa can be directly inspected and biopsied should provide an important indication of the development of malignancy in those patients with longstanding colitis, particularly if the premalignant changes in the rectum noted by Morson and Pang[4] can also be demonstrated in the colon, although in the present group of patients such changes were not seen in the many colonic biopsies.

SUMMARY

Eleven patients, 10 of whom had ulcerative colitis or proctitis of at least 5 years' duration, were examined by double contrast enema and by colonoscopy with multiple biopsies of the colonic mucosa.

Roentgenology underestimated the extent or severity of the disease as assessed by biopsy in 8 out of 11 patients; for example, in 1 patient with roentgenologic evidence of involvement of the ascending and proximal transverse colon, biopsies showed a total colitis. In 2 patients, colonoscopy detected pseudopolyps and polyps which were not revealed by the double contrast barium enema examination.

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GENITOURINARY COMPLICATIONS OF GRANULOMATOUS BOWEL DISEASE*

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REGIONAL enteritis (Crohn's disease) may frequently be associated with genitourinary complications; an incidence of 4–10 per cent has been reported.[11,18] Certain of these complications, such as intestinal-urinary fistula and psoas abscesses, have long been recognized. Others, such as ureteral obstruction and nephrolithiasis, have only recently been emphasized. In most instances, these complications occur in patients whose granulomatous intestinal disease is rather severe and of fairly long duration. Under these conditions, the intestinal involvement may dominate the clinical picture to such an extent that genitourinary complications may not be recognized unless specially searched for. On the other hand, if genitourinary involvement is the initial mode of patient presentation to the physician, the associated gastrointestinal disorder may not be immediately detected. For these reasons, it is important for the radiologist to be aware of all ramifications of this disorder.

In the following, a classification of the genitourinary tract complications of Crohn's disease is presented along with 9 cases which we have recently observed. A brief review of the pertinent literature is also given.

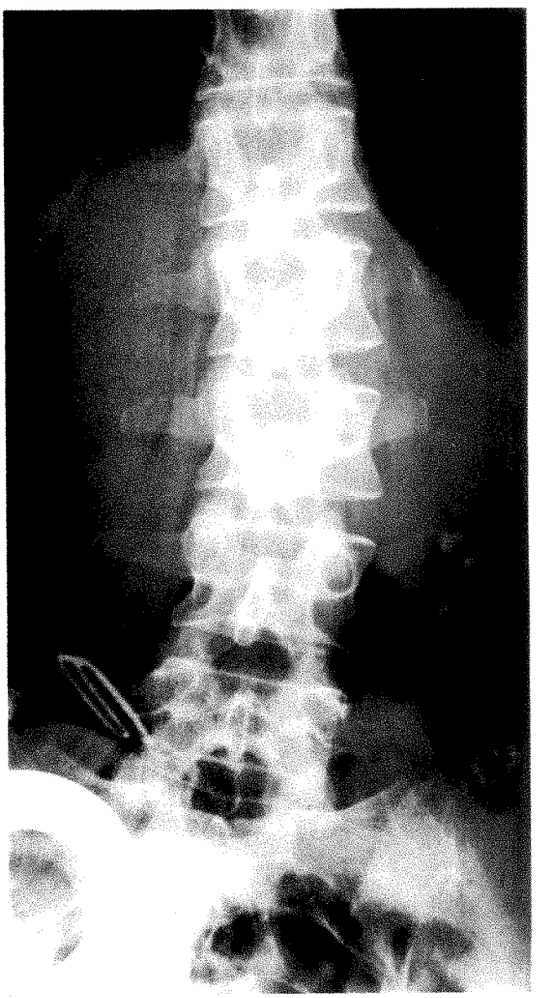


FIG. 1. *Calculi.*

Case 1. Three large calcium renal calculi are seen in the left kidney of this 36 year old female with severe granulomatous colitis and terminal ileitis.

CASE COMMENTS

For the sake of brevity, the pertinent clinical features of our cases are presented in tabular form (Table 1). These cases reflect the wide spectrum of genitourinary complications in regional enteritis: fistula formation is demonstrated in Cases I, II, III and IV; abscess formation in Cases I, II, IV and VII (Fig. 2, *A* and *B*; and 5, *A–C*); ureteral obstruction in Cases V, VI, VII and VIII (Fig. 3, *A* and *B*; 4, *A* and *B*; 5, *A–C*; and 6, *A* and *B*); and renal calculi in Cases I (calcium-base stones, Fig. 1) and IX (urate-base stones). The granulomatous process in all patients who developed genitourinary complications, with the single

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TABLE I

CLINICAL DATA ON 9 PATIENTS WITH CROHN'S DISEASE AND GENITOURINARY COMPLICATIONS

Case	Age (yr.)	Race/ Sex	Length of Disease	Type of Gastrointestinal Involvement	Type of Genitourinary Involvement
I *Fig. 1*	36	Cau. F	6 yr.	Terminal ileum, colon	Calcium renal stones; pelvic abscess; rectovaginal fistula
II *Fig. 2C*	21	Cau. F	10 yr.	Terminal ileum, colon	Enterovesical fistula; pelvic abscess
III	19	Cau. M	1 yr.	Terminal ileum, colon	Enterovesical fistula
IV *Fig. 2, A and B*	31	Cau. F	10 yr.	Terminal ileum, colon	Enterovesical fistula; right lower quadrant abscess
V *Fig. 3, A and B*	24	Cau. M	2 yr.	Stomach, duodenum, terminal ileum	Distal right ureteral obstruction
VI *Fig. 4, A and B*	59	Cau. M	10 yr.	Ileum, colon	Distal right ureteral obstruction with renal atrophy
VII *Fig. 5, A–C*	38	Cau. M	17 yr.	Ileum, colon	Retroperitoneal abscess causing left mid-ureter obstruction and hydronephrosis
VIII *Fig. 6, A and B*	7	Cau. F	8 mo.	Appendix, ileum, colon	Distal bilateral ureteral obstruction with bilateral hydronephrosis and renal failure
IX	48	Cau. F	10 yr.	Terminal ileum, colon	Uric acid stones; pyelonephritis

exception of Case IX, was quite severe. This is in keeping with other patients reported in the literature

DISCUSSION OF CASES AND REVIEW OF LITERATURE

Generally, the genitourinary complications of Crohn's disease fall into 3 broad categories (Table II):

I. Fistula formation between the intestinal tract and urinary tract.

II. Abscess formation in and around the urinary tract.

III. Genitourinary abnormalities other than fistulae and abscesses.

I. FISTULAE

Fistulae formation in patients with Crohn's disease has been well described by Crohn and Yarnis in their text, "Regional Ileitis."[2] From Figure 7, it can be seen that fistulae originate in diseased bowel, usually the ileum. However, the jejunum and colon may also be involved, in which case the fistulae may then extend into the genital organs, the urinary organs, or the soft tissues about either group. Fistulae originating in the ileum, customarily present on the right; when they originate in the jejunum and colon, they are usually on the left.

A. *Urinary.* The most common intestinal-urinary fistulae are the ileovesical fistulae (Cases II, III and IV). In the series of Kyle and Murray,[14] 2 per cent of patients with Crohn's disease developed this type of fistula. Clinically, these patients had pneumaturia and frequency. Attempts to demonstrate the fistulae with air, contrast material or colored solutions in the bladder or rectum were usually unsuccessful. Ginzburg[7] states that the poor visualization of

fistulae by cystography is due to the "valve-like effects of distensible organs," *i.e.*, the bladder. For this reason, Kyle and Murray[14] believe that cystoscopy is the best way to confirm the diagnosis of ileovesical fistula. The male to female ratio in patients with ileovesical fistulae is approximately equal; thus, in the female, the intraabdominal genital organs offer little positional protection to the development of ileovesical fistulae. However, Ginzburg postulates that the uterus does protect the inferior portion of the female bladder from fistulization, making the posterior-superior bladder more susceptible to such fistulae.[7]

Fistulae may also develop between the ileum and the ureters, but this is quite rare.[2]

B. *Genital.* In males, fistulae from the intestines to the genital tract are essentially

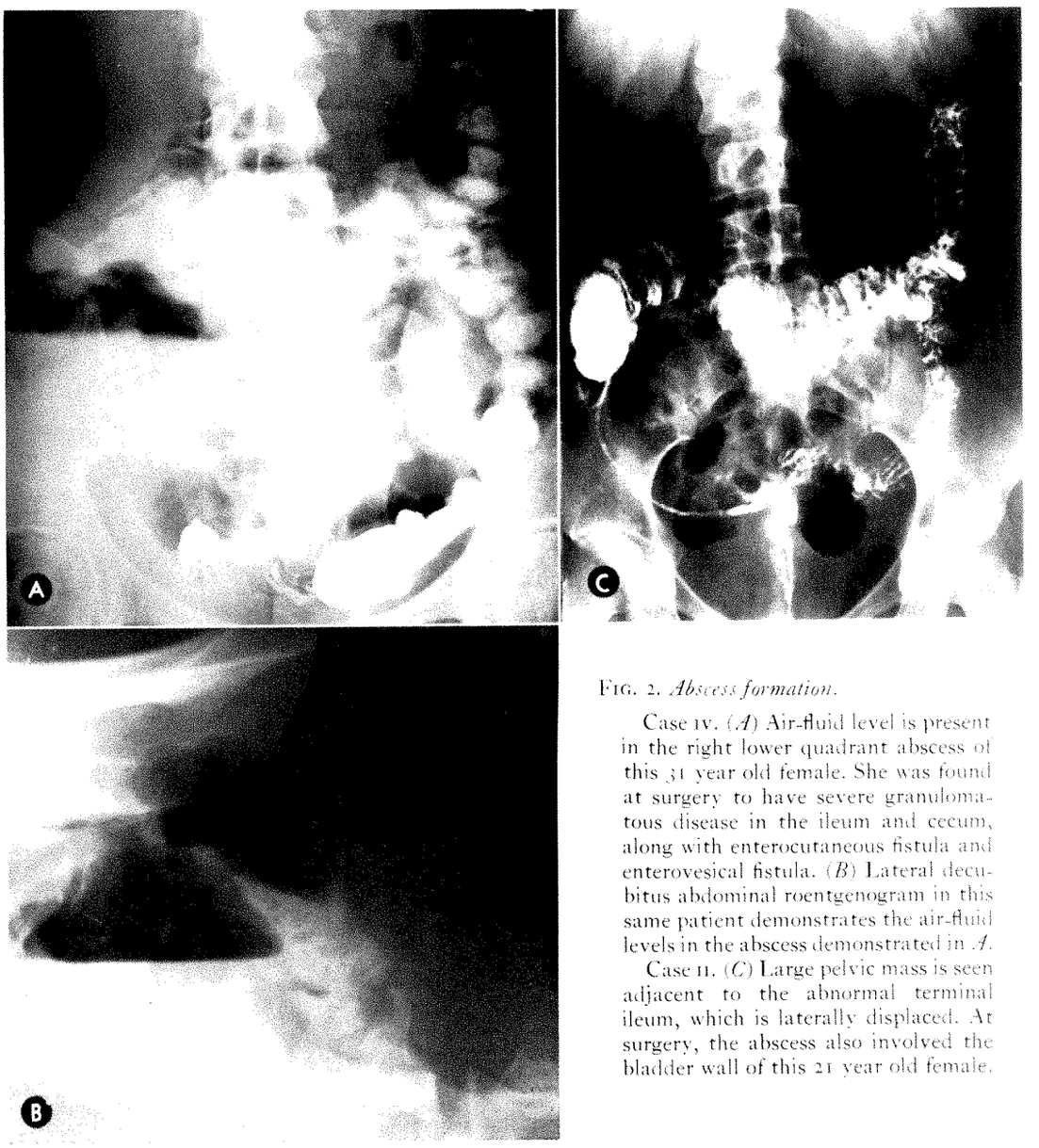


FIG. 2. *Abscess formation.*

Case IV. (*A*) Air-fluid level is present in the right lower quadrant abscess of this 31 year old female. She was found at surgery to have severe granulomatous disease in the ileum and cecum, along with enterocutaneous fistula and enterovesical fistula. (*B*) Lateral decubitus abdominal roentgenogram in this same patient demonstrates the air-fluid levels in the abscess demonstrated in *A*.

Case II. (*C*) Large pelvic mass is seen adjacent to the abnormal terminal ileum, which is laterally displaced. At surgery, the abscess also involved the bladder wall of this 21 year old female.

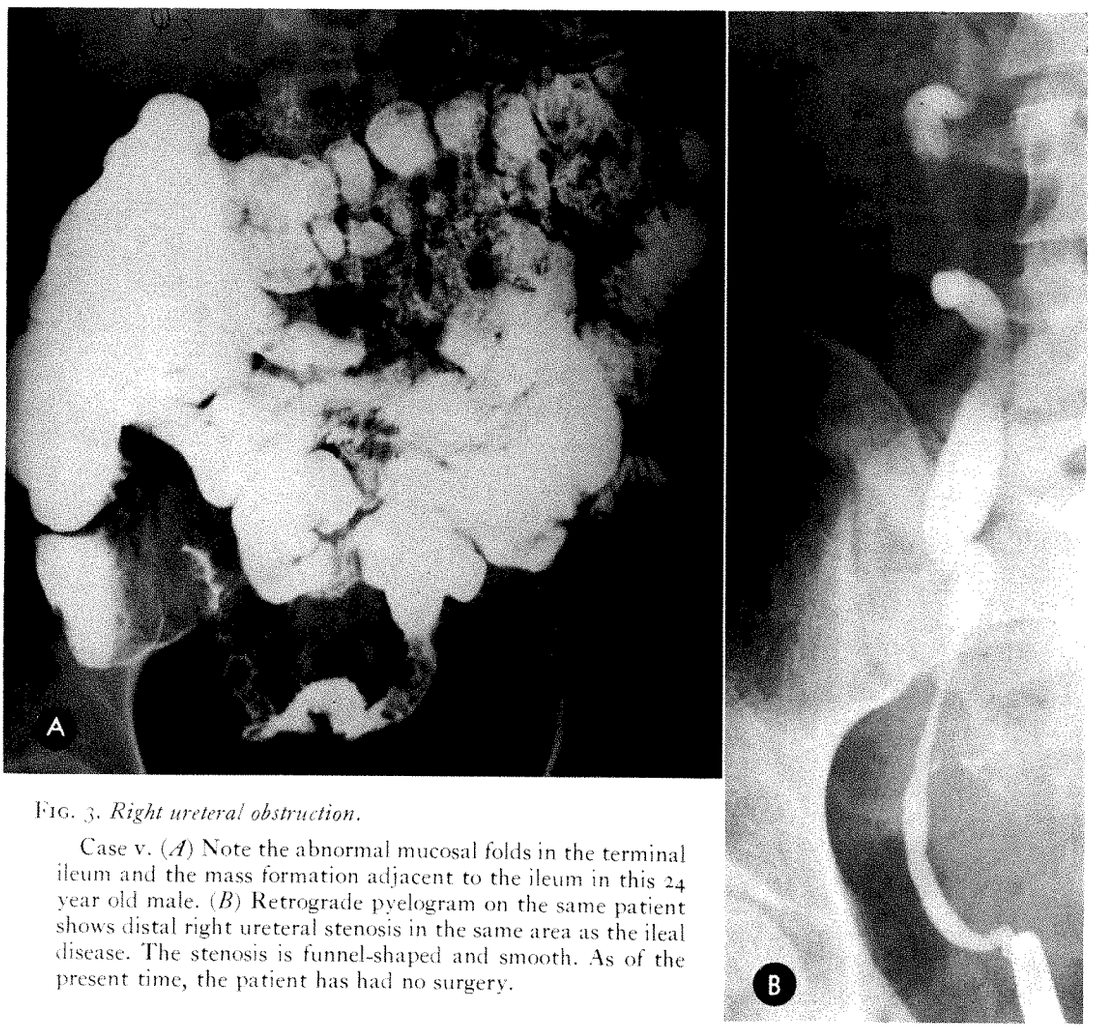


FIG. 3. *Right ureteral obstruction.*

Case v. (*A*) Note the abnormal mucosal folds in the terminal ileum and the mass formation adjacent to the ileum in this 24 year old male. (*B*) Retrograde pyelogram on the same patient shows distal right ureteral stenosis in the same area as the ileal disease. The stenosis is funnel-shaped and smooth. As of the present time, the patient has had no surgery.

nonexistent. In females, 12 cases of ileovaginal fistulae have been reported in the literature,[13] and an occasional case of fistula to the uterus[13] and fallopian tubes[2] has been reported. Rectovaginal fistula may also be seen in patients with Crohn's disease (Case 1).

II. ABSCESS

Abscess formation in patients with Crohn's disease may occur in locations that affect the urinary tract anywhere from the kidney to the bladder (Fig. 8).

A. *Kidney.* Ginzburg[7] recently reported 5 regional enteritis patients who developed perirenal abscesses. Clinically, these lesions resembled perinephric abscess, and in 3, the intravenous pyelograms were normal. This has led the author to recommend that barium enema examination, upper gastrointestinal series, and small bowel series be done in patients with retroperitoneal abscess and normal intravenous pyelogram, specifically to search for Crohn's disease.

B. *Ureter.* Psoas abscess in regional enteritis may cause deviation or obstruction of the ureters. Of 5 cases of psoas abscess reported by Kyle,[15] 3 occurred on the right side as a result of terminal ileitis and 2 occurred on the left side, 1 as a result of regional jejunitis and 1 as a result of granulo-

matous colitis. Roentgenograms of the abdomen (Fig. 2, *A* and *B*) showed a bulging psoas shadow, psoas mass, gas within the psoas mass and gas dissecting into the groin, resembling an inguinal hernia containing intestine. Contrast studies may demonstrate ureteral deviation, ureteral obstruction or fistula formation. The differential diagnosis should principally include appendicitis, diverticulitis, tuberculosis and neoplasm.

C. *Bladder.* Pelvic abscess (Fig. 2*C*) may cause ureteral obstruction, unilateral or bilateral, or bladder deformity.[7] The abscess may even extend into the wall of the bladder itself causing a filling defect on the contrast studies.

III. URINARY COMPLICATIONS IN REGIONAL ENTERITIS, EXCLUSIVE OF FISTULA AND ABSCESS

The urinary complications of regional enteritis, exclusive of fistula formation and abscess formation, fall into 2 general categories. The first category consists of changes that occur in the kidney not as a result of direct extension of Crohn's disease from the gastrointestinal tract, but rather as a result of some metabolic aberration in these patients. The second category includes abnormalities of the ureter and bladder which occur as a direct result of

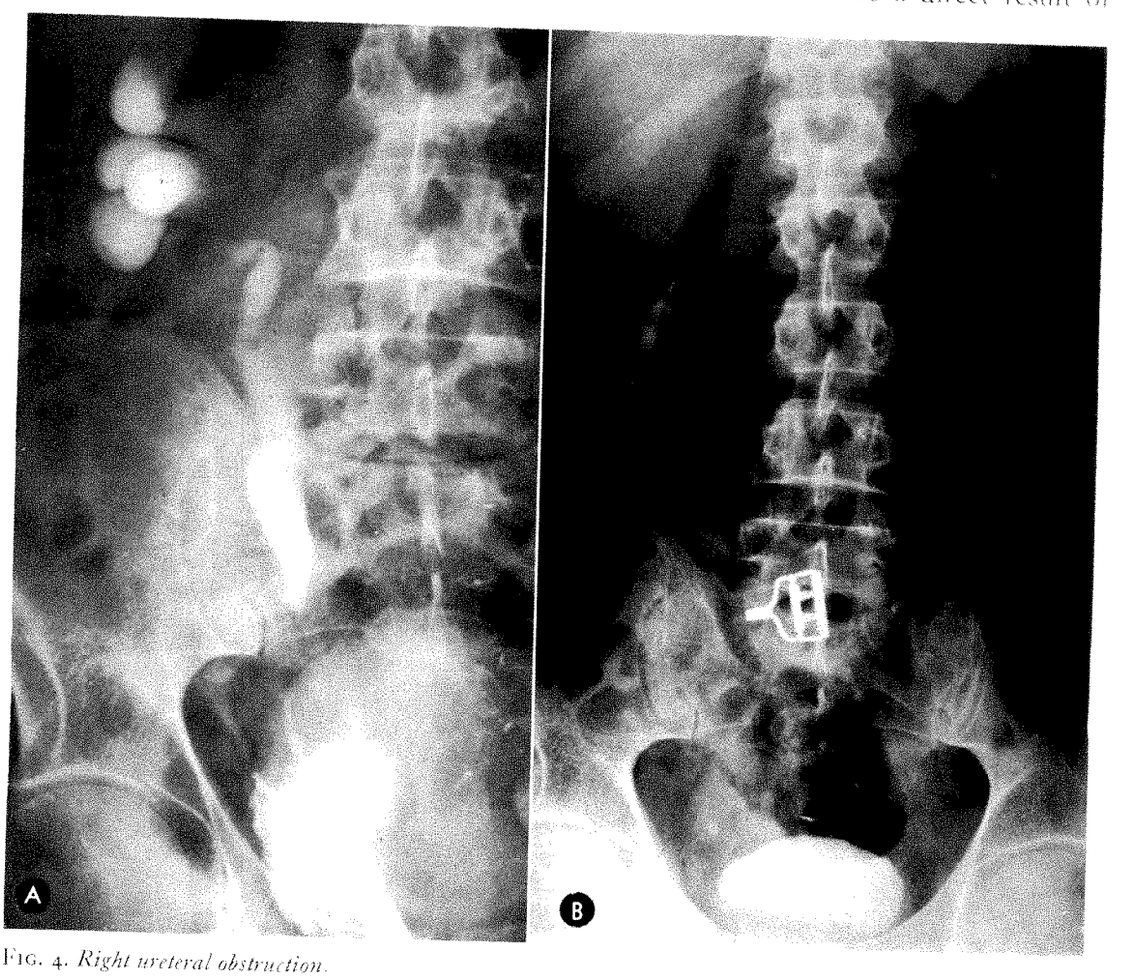


FIG. 4. *Right ureteral obstruction.*

Case VI. (*A*) Distal right ureteral stenosis shown at the time of surgery to be due to retroperitoneal fibrosis in this 59 year old male. (*B*) Note the marked right renal atrophy (secondary to prolonged hydronephrosis) in this same patient.

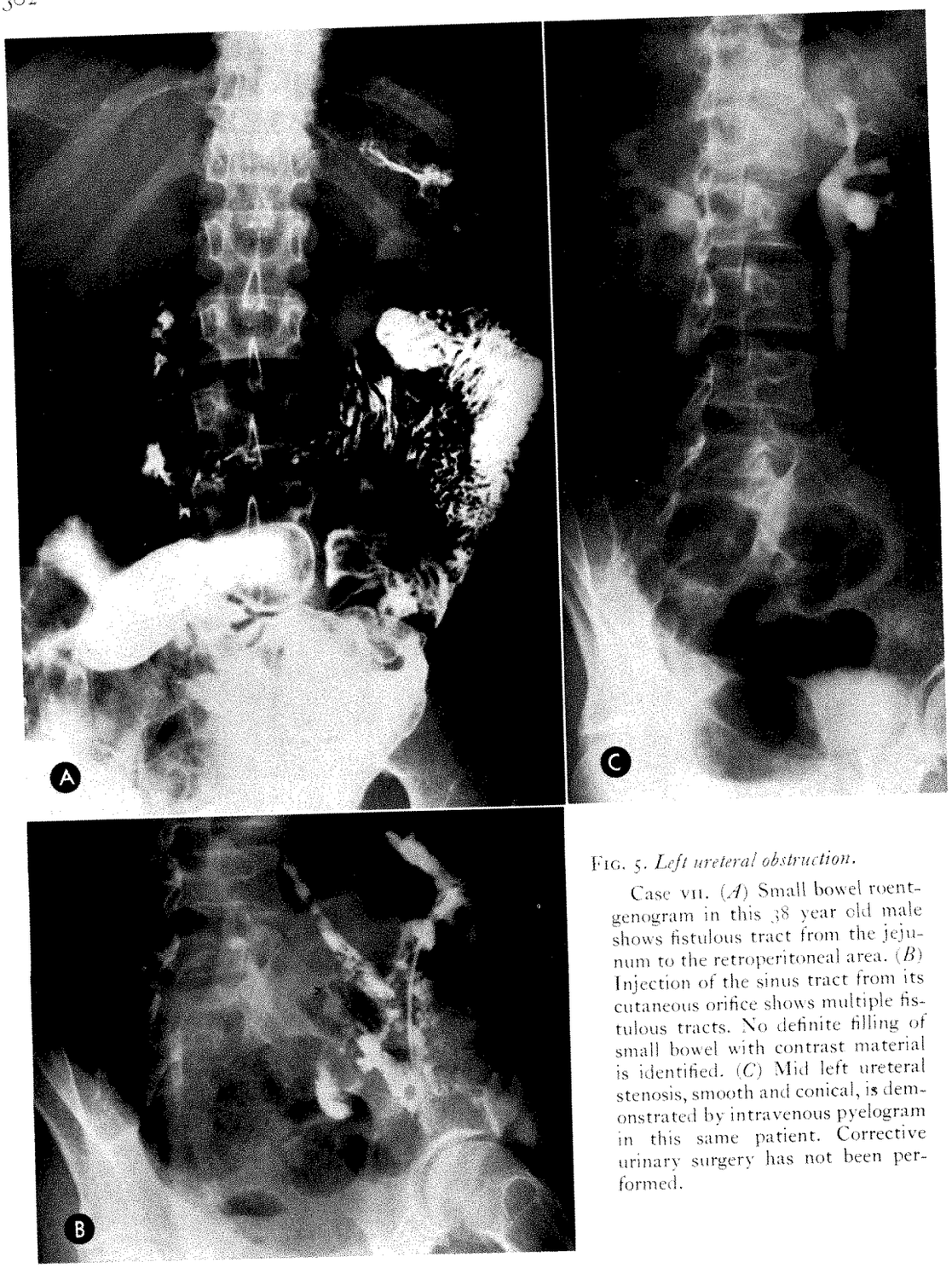


Fig. 5. *Left ureteral obstruction.*

Case VII. (*A*) Small bowel roentgenogram in this 38 year old male shows fistulous tract from the jejunum to the retroperitoneal area. (*B*) Injection of the sinus tract from its cutaneous orifice shows multiple fistulous tracts. No definite filling of small bowel with contrast material is identified. (*C*) Mid left ureteral stenosis, smooth and conical, is demonstrated by intravenous pyelogram in this same patient. Corrective urinary surgery has not been performed.

extension of the disease process itself, *i.e.*, from spreading fibrosis (Fig. 9).

A. *Kidney.* 1. Mild. Certain pathologic changes in the kidneys have been reported by Chapin *et al.*[1] in patients with regional enteritis; such changes were discovered only at autopsy and, generally, had no ap-

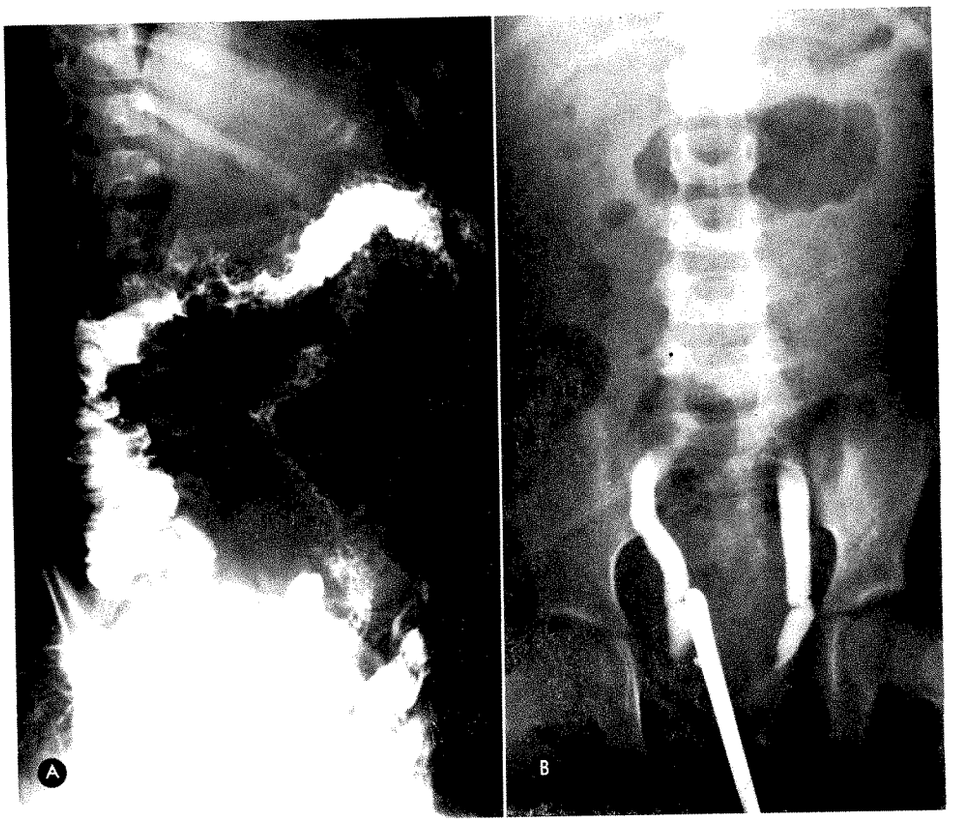


FIG. 6. *Bilateral ureteral obstruction.*

Case VIII. (*A*) This 7 year old female has ileal and colon involvement with the most severe disease being in the transverse colon. (*B*) Bilateral retrograde ureteral injection shows distal obstruction. Renal biopsy showed changes consistent with prolonged hydronephrosis. This child has had no surgery; thus, the ureteral obstructions are proved to be due to the granulomatous bowel disease. Certainly, a congenital lesion remains a very real possibility.

parent clinical manifestations. They consisted of glomerulitis and mild tubular disease—findings considered nonspecific and occurring in many patients with acute and chronic disease. Hydropic degeneration of the proximal convoluted tubule was described in 4 of 39 patients; this finding may also be seen in chronic ulcerative colitis, causing the authors of that report to believe that there may be some, as yet unknown, association between this lesion and chronic intestinal disease.[1]

2. Nephrolithiasis. The incidence of renal calculi is higher in patients with Crohn's disease than it is in the general population. Deren *et al.*[3] report an incidence of 6.3 per cent and Grossman and Nugent[10] report an incidence of 3.6 per cent in their group of patients. This contrasts with the figure of 0.9 patients with "stones" per 1,000 patients admitted to the general hospital population.[10]

The relationship of surgery to these Crohn's disease patients with calculi has been evaluated; 88.6 per cent had resection of small and/or large bowel.[10] In addition, Grossman and Nugent[10] state that the incidence of stones in this group increases following excisional surgery from 3.6 to 4.4 per cent. This compares to the series of Deren *et al.*[3] in which the reported increased incidence of renal calculi in Crohn's disease patients who had an ileostomy procedure was 4.8–7.4 per cent. Surgical intervention for the removal of the calculi is frequently necessary in this group.[10]

TABLE II

GENITOURINARY COMPLICATIONS OF CROHN'S DISEASE

I. *Fistula*
  A. Urinary
    1. Ileum or colon to ureter
    2. Ileum or colon to bladder
  B. Genital
    1. Ileum to fallopian tube
    2. Ileum to uterus
    3. Ileum or rectum to vagina
II. *Abscess*
  A. Renal or retroperitoneal
  B. Ureteral or periureteral
  C. Vesical or pelvic
III. *Genitourinary complications exclusive of abscess and fistulae*
  A. Renal or metabolic
    1. Mild or nonclinical
      a. glomerulitis
      b. tubular disease
      c. hydropic degeneration of proximal convoluted tubule
    2. Nephrolithiasis
    3. Amyloidosis
  B. Ureteral obstruction secondary to Crohn's disease of the retroperitoneal area
  C. Bladder abnormalities secondary to extension of Crohn's disease to this area

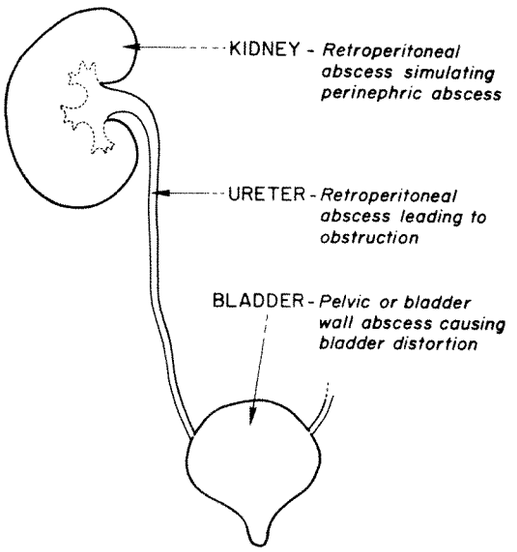


FIG. 8. Perigenitourinary abscess formation in Crohn's disease.

In the general population, the renal calculi may be formed on a base of either uric acid (Case IX) or calcium (Case I, Fig. 1). In the normal population, 5–15 per cent of renal stones form on an uric acid base; however, in the patients with Crohn's disease, 59 per cent of renal stones are uric acid calculi.[3] This increased incidence of uric acid stones is believed related to the chronic diarrheal state, which results in

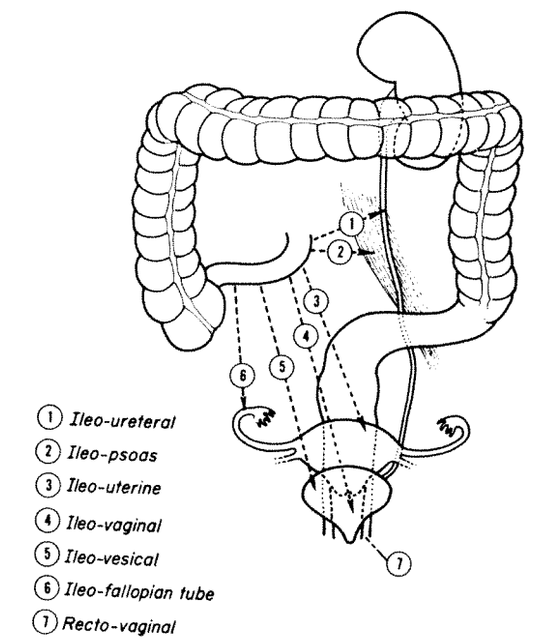


FIG. 7. Genitourinary fistula formation in Crohn's disease.

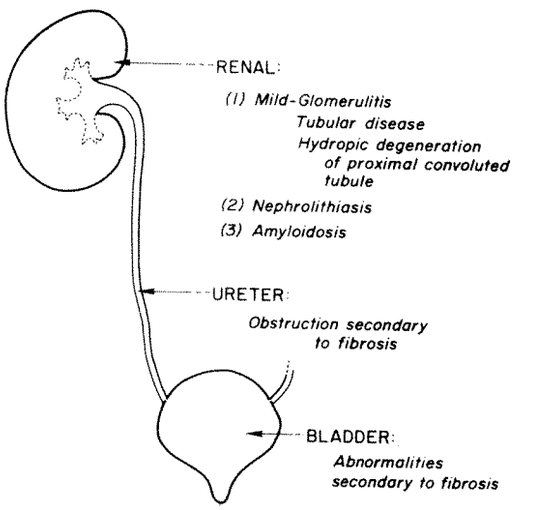


FIG. 9. Urinary complications in Crohn's disease exclusive of abscess and fistula.

excessive loss of basic ions from the gut. As a consequence, the serum and the urine become more acidic, with the urine pH approaching 5.0. At a pH of 5.0, 75 per cent of uric acid is in the free rather than the salt form and, as such, it is much less soluble. Furthermore, a second important factor is chronic water loss secondary to the diarrhea, which causes the urine to be more concentrated, with the specific gravity often being consistently higher than 1.020.[3] Hence, any clinical situation such as ileostomy or exacerbation of the disease that causes an increased fluid loss may result in increased urinary uric acid crystals and thus, calculus formation.[6]

Development of calcium-base stones may be related to a combination of recumbency and steroid therapy, which increases the urinary calcium excretion (Fig. 1).[6]

In conclusion, renal calculi which develop in patients with regional enteritis will more likely be nonopaque uric acid stones than opaque calcium stones. Patients with low urine pH (5.0) and high urine specific gravity (1.020) may be candidates for uric acid stone development.

3. Amyloidosis. Amyloidosis, essentially following a secondary distribution pattern, may be seen in patients with Crohn's disease;[21,22] when deposits are in the renal glomeruli, they can produce the nephrotic syndrome. The diagnosis of amyloidosis is rarely made ante mortem and the development of such in the series of Wallenstein *et al.*[21] could not be related to the duration of the disease, the extent of the disease, the degree of suppuration, the treatment with steroids or the formation of fistulae.

B. *Ureter.* Ureteral deviation or obstruction in patients with regional enteritis may result either from abscess formation (Fig. 5, *A–C*) or from retroperitoneal fibrosis (Fig. 3, *A* and *B*; and 4, *A* and *B*), secondary to Crohn's disease. Symptoms, which are rarely present, consist of frequency, dysuria, or pain in the hips, anterior thigh or flank. In retrospect, some of the patients in the series of Present *et al.*[16] remembered flank pain associated with fever. Very few of the patients with obstructive uropathy will have objective evidence of urinary infection.

Roentgenographically, obstruction of the ureter usually occurs at the level of the pelvic brim and is usually unilateral. Bilateral involvement should suggest pelvic abscess or some other possible etiology, as in Case VIII (Fig. 6, *A* and *B*). The right ureter is frequently involved due to its proximity to the terminal ileum (Fig. 3, *A* and *B*; and 4, *A* and *B*). Left ureter involvement is much less common. If obstruction is present on the left and is in the proximal ureter, the diseased bowel segment is usually the jejunum (Fig. 5, *A–C*); conversely, if the left ureteral obstruction is in the distal ureter, the diseased bowel segment is usually the distal colon. The intravenous or retrograde pyelogram may show ureteral deviation or obstruction.[4,8,11,16–20] The area of stenosis is usually symmetrically tapered and cone-shaped, indicating a periureteral process (Fig. 3, *A* and *B*; 4, *A* and *B*; and 5, *A–C*). If the obstruction is of long duration, the dilated ureter will usually have a more tortuous course. When no ureteral dilatation is present but when the degree of fixation of the ureter must be known, Present *et al.*[16] recommend a double exposure film of the abdomen in deep inspiration and deep expiration.

On the other hand, Schofield *et al.*[20] have recommended renography rather than pyelography to evaluate patients with ureteral obstruction secondary to Crohn's disease. However, the initial evaluation of patients with genitourinary problems and Crohn's disease should still be by pyelography, since more precise information is gained.

The surgical approach in these patients is variable. Usually, treatment of the diseased bowel segment will result in relief of the obstruction. Bypass surgery or bowel resection may be necessary. Recently, surgeons have encouraged ureterolysis procedures in association with bowel resection. If renal failure is too advanced, nephrectomy may be necessary.

In short, due to the increasing frequency of recognition of ureteral obstruction in patients with Crohn's disease, intravenous urography is recommended for the study of urinary symptoms, severe granulomatous disease, and prior to bowel resection.

C. *Bladder.* Patients with bladder involvement may be symptomatic or asymptomatic. Such involvement may be the result of adhesions adjacent to and involving the bladder wall;[9] wall granulomas may even be present. Contrast studies may reveal bladder wall deformity secondary to adhesions or bladder filling defects secondary to granulomas.

SUMMARY

A general review of genitourinary complications in patients with Crohn's disease is presented along with 9 new cases, the roentgenographic findings of which are evaluated.

It would seem that a high incidence of such complications is present in this patient group; hence, evaluation of the genitourinary tract by means of intravenous pyelography is recommended in any regional enteritis patient with urinary symptoms, advanced disease, or anticipated bowel resection.

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RETRORECTAL CYSTS OF DEVELOPMENTAL ORIGIN*

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RETRORECTAL cysts of developmental origin are rare. They have been the subject of scattered reports since 1885 when Middeldorpf[17] described a tumor posterior to the rectum that was comprised solely of intestine. Although Middeldorpf's patient was a 1 year old girl, most of the subsequently described patients have been adults. These unusual congenital cysts are of several histologic types, the most important being squamous-lined (dermoid or epidermoid) cysts, postanal gut (tail gut) cysts, and rectal duplications (enteric or enterogenous cysts, enterocystomas). All have well defined and essentially similar clinical features. However, their roentgenographic characteristics, with the exception of brief mention in a few reports, have not previously been described.

The purpose of this paper is to record 4 cases of developmental retrorectal cysts in adults in which roentgenographic contrast studies were obtained. The roentgenographic features will be discussed and the clinical presentation, pathology, and embryology will be briefly reviewed.

REPORT OF CASES

CASE I. L.M., 210-96-31, a 30 year old female, was told of a rectal tumor discovered during delivery of her third child. She was asymptomatic. Two years later, at Columbia-Presbyterian Medical Center (CPMC), rectal examination revealed a 4×3 cm. mass in the posterior midline at the level of the anorectal ring. Anoscopy demonstrated a bulge posteriorly with normal overlying mucosa. Needle aspiration yielded sterile chocolate-colored material.

Barium enema examination revealed a smooth intramural or extrinsic mass effect on the posterior rectum. The sacrum and coccyx were normal (Fig. 1, *A* and *B*).

The patient underwent excision of a 3×2×2 cm. cystic mass which appeared to be intramural in the rectum and extended to the region of the coccyx. The main cyst lacked an epithelial lining, but was bordered by chronically inflamed granulation tissue including large numbers of lipid-laden macrophages. Elsewhere in the tissue, several other smaller cysts were noted; most of these were lined by stratified squamous epithelium, but one collapsed cyst had a lining epithelium which varied from stratified squamous, to transitional, to ciliated columnar in type, interspersed with several mucus-producing goblet cells (Fig. 2).

The pathologic diagnosis was postanal gut cyst, inflamed.

CASE II. V.T., 201-71-93, a 27 year old female, developed a right perirectal abscess following the birth of her first child. Over the ensuing 3 years, she had recurrent perirectal abscesses that required incision and drainage.

The patient was admitted to CPMC and underwent drainage of an infected retrorectal cyst and excision of a tiny fistula between cyst and rectum. Microscopically, the specimen was lined by stratified squamous epithelium with focal chronic inflammatory cell aggregates and prominently dilated lymphatics in the underlying fibrous stroma. Two layers of smooth muscle were noted more deeply in the wall of the structure. A second fragment represented rectal mucosa which led to a fistula lined by granulation tissue, which in turn communicated with the squamous-lined structure.

Three and 5 months postoperatively, sinograms were obtained *via* a mushroom catheter placed in a tract that opened between the anus and the coccyx. A retrorectal cystic cavity with a fistula to the rectum was demonstrated (Fig. 3, *A* and *B*).

Six months postoperatively, excision of a 6×5 cm. cystic fluid-filled retrorectal mass was performed. It extended from the anal sphincter to the 3rd sacral segment and anteriorly to the right to the posterior wall of the vagina. The mass was lined by whitish tissue with occasional reddish polypoid elevations. The sac lining con-

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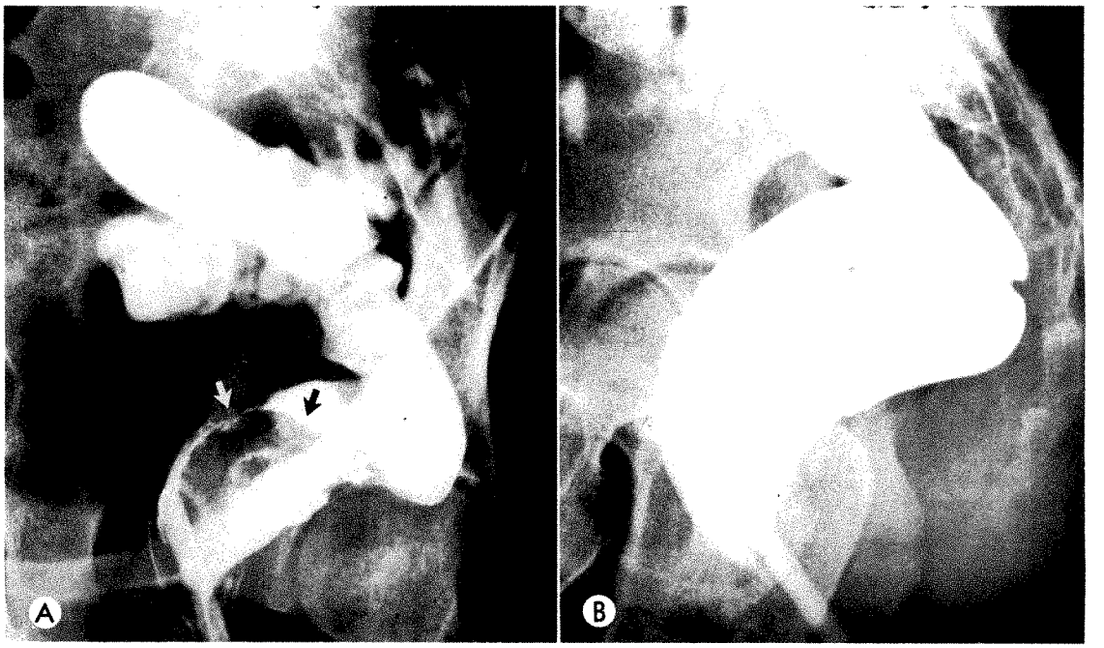


FIG. 1. Case 1. *Postanal gut cyst.* Barium enema roentgenograms demonstrate: (*A*) incompletely and (*B*) fully distended rectum. A smooth mass (arrows) indents the posterior aspect of the rectum anterior to the coccyx. The rectal mucosa is intact. The sacrum and coccyx are normal.

sisted of stratified squamous epithelium except where it had become ulcerated and was replaced by granulation tissue. Moderate chronic inflammation was noted in the underlying stroma. There was a considerable amount of scarring in the wall which had partly obliterated the muscle coats. The deep aspect of the sac was formed by fibro-adipose tissue with an outer surface resembling serosa. However, no definite mesothelial cell layer could be demonstrated.

The pathologic diagnosis was duplication of the rectum.

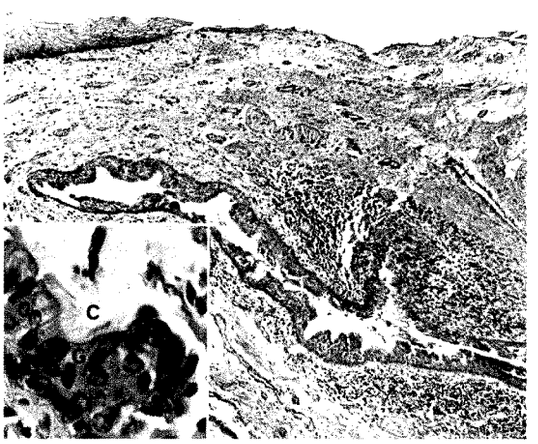


FIG. 2. Case 1. *Postanal gut cyst.* Partly collapsed cyst, lined variously by stratified squamous and ciliated columnar epithelium as well as by a transitional type of epithelium. The upper part of the field shows another locule of the lesion, having a lining of pure squamous epithelium (mucicarmine ×25). *Insert.* Higher magnification to show cilia (C) and mucicarminophilic goblet cell (G) (mucicarmine, oil immersion ×400).

CASE III. N.B., 84-70-86, a 20 year old female, developed an abscess near the tip of the coccyx. Surgical drainage was performed first through the rectum and later through the overlying skin.

Five years later, an abscess posterior to the rectum was drained of about 15 cc. of pus and the perirectal cysts were excised.

Two months later, the patient presented with an acutely inflamed retrorectal cyst and drainage of pus through the rectum. Sinography was performed *via* a catheter passed into a fistulous tract in the wall of the rectum. The contrast material outlined a pocket behind the rectum just inferior to the coccyx which was separate from the acutely inflamed cyst. The inflamed cyst was excised. Microscopic examination

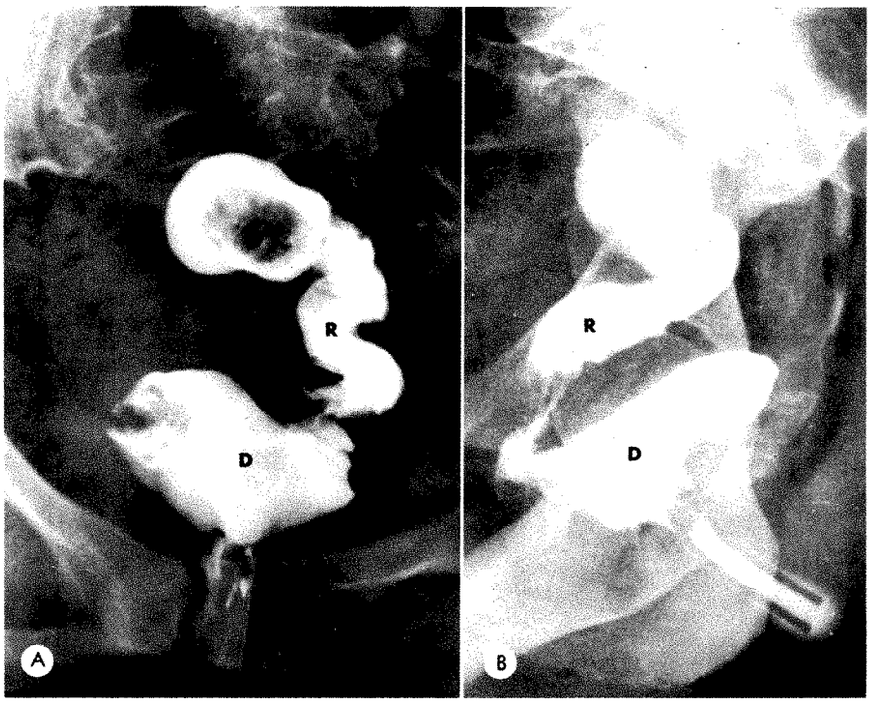


Fig. 3. Case II. *Rectal duplication.* (*A*) Anteroposterior and (*B*) lateral views from a sinogram. A sinus tract containing a catheter extends from the cystic duplication to the skin between the anus and the coccyx. Contrast material injected through the catheter fills the duplication (D) located in the retrorectal space. Contrast material passes from the duplication into the rectum (R) *via* a fistulous communication. The sacrum and coccyx are normal.

showed the fragments to be lined by stratified squamous epithelium. The underlying fibromuscular wall was heavily infiltrated by both acute and chronic inflammatory cells associated with recently extravasated blood.

One year later, a 2 cm. cyst of the posterior wall of the rectum just below the tip of the coccyx was excised (slides no longer available).

The pathologic diagnosis was a cyst of congenital origin lined by stratified squamous epithelium.

Case IV. J.R., 100-76-09, a 61 year old male, underwent hemorrhoidectomy. Subsequently, he developed an ischiorectal abscess that required incision and drainage. One year later, an attempted repair of a perirectal fistula was unsuccessful because of copious hemorrhage.

Six years later, he exhibited an area of scar and a sinus opening to the skin in the left posterolateral perirectal region. A sinogram demonstrated a 5 cm. tract in the midline posterior to the anus and rectum extending to the region of the coccyx.

Excision of the 3×4 cm. retrorectal cyst with its sinus tract was performed. Microscopically, the fragments were lined by keratinizing stratified squamous epithelium resting on a heavily inflamed fibrous wall. No muscle was observed. In some fragments, probably representing sinus tract, the lining epithelium was absent and had been replaced by chronically inflamed granulation tissue. The coccyx was also inflamed.

The pathologic diagnosis was a cyst lined by stratified squamous epithelium with inflammatory changes.

PATHOLOGY

The classification of cysts in the retrorectal region is dependent largely on the type of epithelium found therein. Thus dermoid cysts are lined by stratified squamous epithelium and contain dermal appendages (hair follicles, sebaceous glands and/or sweat glands) in the wall closely associated with or actually communicating

with the cyst lining. In order to make a diagnosis of "teratoma," derivatives of all 3 germ layers must be represented.

Enteric cysts or duplications are lined by squamous or glandular epithelium of intestinal type, but, in addition, contain one or more layers of smooth muscle in their walls. Some enteric cysts are covered by a serosal layer.

Cysts of the postanal gut are lined by cuboidal to columnar epithelium and contain mucin-secreting goblet cells. They lack the muscular and serosal layers found in duplications and lack skin appendages, thus ruling out dermoid cysts. These criteria were set forth by Peyron[20] in 1928, and have been fulfilled in Case 1 reported above (Fig. 2). Some portions of postanal gut cysts may be lined by transitional or even squamous epithelium.[6,29] Some of the columnar cells in our Case 1 were ciliated; this change has been previously described by Gius and Stout,[7] Willis,[29] and Ewing.[6] The latter pointed out that undifferentiated epithelium in embryologic life is often ciliated, so that it is not surprising that a cyst of displaced or retained embryonic remnants includes ciliated cells.

Many of the reported instances of retrorectal cysts, as well as the majority of those reviewed in this hospital, were lined by stratified squamous epithelium. It is extremely difficult to classify these as to their precise origin if they lack the characteristic features of the lesions discussed above. In the opinion of the authors, a squamous lining may represent the end result of a previously inflamed cyst, whose lining had broken down and which healed by becoming lined by a metaplastic squamous epithelium. Such was undoubtedly the situation in our Case 1. Some squamous-lined cysts probably represent implantation of epithelium either during fetal life or at the time of a prior surgical procedure.

EMBRYOLOGY

Postanal gut cysts, as the name implies, are believed to originate from persistent remnants of the embryonic postanal or tail gut. The postanal gut, a part of the hindgut, is present during the 3.5 to 8.0 mm. stage of development at a time in which the embryo possesses a true tail (Fig. 4). Normally, the postanal gut fills with epithelial debris and completely disappears. However, if regression is incomplete, persistent tissue may give rise to cysts in the retrorectal space.[7,20]

Several theories have been proposed to explain the embryologic basis for intestinal duplications. Duplications have been considered to be derived from: intestinal diverticula normally present during the second month of embryonic life[13]; sequestered epithelium in the embryonic intestine[9]; abnormal coalescence of the vacuoles normally present during the solid stage of embryonic intestinal development[2]; "adhesions" connecting the developing gut and neural tube[16,26]; and partial twinning of the caudal end of the body.[25]

Retrorectal cysts lined by stratified squamous epithelium are generally thought to be of developmental origin, although their precise embryologic basis is unknown. Virtually every structure found in the caudal region of the embryo has been mentioned as a possible origin for such cysts. These include the proctodeal membrane, coccygeal vestiges, the neurenteric canal,

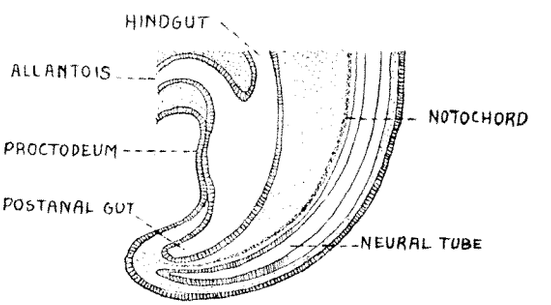


FIG. 4. Diagrammatic sagittal section through the caudal portion of a 4 mm. human embryo (modified from Peyron[20]). The embryo possesses a true tail at this stage. The postanal gut is a part of the hindgut extending into the tail. It lies caudad to the proctodeum, the site of the future anus. The postanal gut normally disappears as development progresses. Abnormally persistent remnants are thought to give rise to postanal gut cysts.

the postanal gut, and ectodermal inclusions formed during faulty coalescence of cutaneous surfaces in embryonic life.[8,15,28] The subject is complicated by the identification, as mentioned above, of stratified squamous epithelium lining portions of rectal duplications or postanal gut cysts.[7,11,20]

ROENTGENOGRAPHIC FEATURES

The uncomplicated developmental cyst appears as a soft tissue mass in the retrorectal space. Barium enema examination reveals a smooth indentation of the posterior wall of the rectum near the anorectal junction. The overlying rectal mucosa is intact (Fig. 1, *A* and *B*). With rare exceptions, the mass contains no calcium and the sacrum and coccyx are normal. Most reported cysts have been less than 12 cm. in diameter.

Retrorectal developmental cysts often become infected. They may then present with a draining sinus opening onto the perianal skin between the anus and the coccyx. Alternatively, the cyst may communicate *via* a fistulous tract with the anus, rectum, or very rarely, the vagina. In these cases, the barium enema study may disclose no mass effect, since the cyst is continuously drained of its contents and is therefore small. Injection of contrast material into the sinus tract outlines a cystic cavity which lies anterior to the coccyx and which may extend cephalad to the level of the mid-sacrum. Fistulous connection with the rectum or anus may be demonstrated (Fig. 3, *A* and *B*).

DISCUSSION

Congenital cysts of the retrorectal space are rarely diagnosed. In one reported series of 20,851 proctoscopies, only 3 such cases were discovered. Although developmental cysts may present at any age and in either sex, most have been in adult females. The majority of patients have no symptoms. Typically, a retrorectal mass is discovered during a routine physical examination or during childbirth. However, a significant minority of patients have symptoms secondary to infection in the cyst. A frequently elicited history is that of recurring retrorectal abscesses and repeated operations for anal fistulae. A small group of patients having large cysts experience symptoms of rectal fullness or pressure.[22]

The roentgenographic features of developmental retrorectal cysts in adults have heretofore received only scant attention in the literature. Findings on plain roentgenograms of the sacral region have been mentioned in several reports and have usually been normal. However, cases having sacrococcygeal anomalies,[1,15,21,27] anterior sacral erosions,[10] and soft tissue calcification have been described.[14,15] A partially calcified mucin-secreting adenocarcinoma arising in the wall of an enterogenous cyst has been reported.[3] Hanley and Hines,[8] in an account of 8 cases of presacral epidermoid cysts, mention a soft tissue mass seen on barium enema examination. A case report by Perkins and Chaffee[19] illustrates a barium enema roentgenogram in which the rectum is narrowed and displaced laterally. Sinus tract studies have been mentioned by several authors.[11,21,23,27]

A number of mass lesions may arise in the retrorectal space and the roentgenograms may provide important clues in the differential diagnosis. For example, chordomas may arise in the sacrococcygeal region. Unlike congenital cysts, however, chordomas are usually associated with bone destruction, and, in about 50 per cent of cases, soft tissue calcification.[24] Sacrococcygeal teratomas also may contain calcification, but usually occur in infants.[5] An anterior sacral meningocele is readily diagnosed by myelography and may be suspected on the basis of an anomalous sacrum.[12] Rectal leiomyosarcomas may simulate the deformity produced by a congenital cyst, but occasionally may be distinguished because of mucosal involvement with ulceration and bleeding.[18] The same is true of cloacogenic carcinomas. Several other tumors, including neurofibromas, ependymomas, and osteogenic sarcomas, may rarely present in the retrorectal space.

Their nature may be suspected on the basis of clinical findings and roentgenograms of the sacrum and coccyx.

The demonstration of a retrorectal cystic cavity by injection of contrast material into a sinus tract should suggest the possibility of an infected developmental cyst. This is particularly so in the setting of repeated operations for an anal fistula, recurring retrorectal abscesses, and inability to find a primary source of infection at the usual site in a crypt at the dentate margin.[22]

Because of the high predilection to infection (15 of 38 cysts were infected in one series), the preferred treatment of retrorectal cysts is complete excision. Removal is recommended also because of occasional cases of malignancy arising in developmental cysts. Both squamous cell and adenocarcinoma have been reported.[1,3,4,22]

SUMMARY

Developmental retrorectal cysts presenting in adults are discussed.

Three types are identified on histologic grounds: postanal gut cysts; rectal duplications; and squamous-lined cysts. Despite differing histology and embryologic origin, all are clinically and roentgenographically similar.

Developmental cysts typically present in one of two ways. Barium enema examination may reveal a smooth mass effect on the posterior rectal wall anterior to the coccyx and lower sacrum. Alternatively, infected cysts frequently develop fistulous tracts to the rectum and to the skin between the anus and coccyx; these may be demonstrated on sinograms.

Roentgenograms may aid in differentiating developmental cysts from other mass lesions of the retrorectal space.

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ANGIOGRAPHIC FINDINGS IN PNEUMATOSIS CYSTOIDES INTESTINALIS*

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PNEUMATOSIS cystoides intestinalis is a rather uncommon disease. In spite of the fact that the condition has been known for more than 200 years, the etiology is still undetermined. A large number of papers concerning the subject have been published, both clinical and experimental. Among these, the most comprehensive paper was published by Koss,[3] who made a review of 255 cases collected from the literature, adding 1 of his own.

The diagnosis is usually made at a roentgen examination of the abdomen, the small bowel or the colon, and the findings are discovered accidentally, most often not related to the symptoms of the patient. Pneumatosis cystoides intestinalis has a benign course and does not call for treatment unless complications occur, *e.g.*, in the form of intestinal obstruction or by persistent or recurrent pneumoperitoneum.

We have had the opportunity to observe 2 patients with pneumatosis cystoides intestinalis during the last few years; both patients were examined with angiography of the bowel.

Angiography seems not to have been performed previously in this condition and since the etiology is still obscure, we believe it worthwhile to report the findings.

REPORT OF CASES

Case I. A 65 year old woman was admitted to the hospital with a 4 day history of right upper abdominal pain. She had no symptoms of bowel distress. At examination a slight tenderness on palpation of the right upper abdominal quadrant was found. The temperature was 38.2°C., the leukocyte count 9,100/mm.^{3}, hemoglobin 14.8 gm./100 ml., serum bilirubin 0.9 mg./100 ml. and the erythrocyte sedimentation rate 26 mm./hour. The urine was normal. The patient was kept under observation, her symptoms subsided, and 24 hours later she was without symptoms and quite well again. Roentgen examinations of the esophagus and the stomach were performed which were normal. Cholecystography revealed a 3×4 cm. calculus. A barium enema study showed gas-filled cysts in the wall of the splenic flexure of the colon, where the cysts produced broad-based impressions on the lumen of the bowel (Fig. 1*A*), whereas other parts of the colon were normal. Two weeks later angiography of the superior and inferior mesenteric arteries was done (Fig. 1*B*). No pathologic changes were seen within the superior mesenteric artery and its branches. The inferior mesenteric artery and its branches were of normal diameter and no irregularities were seen. In the splenic flexure the distance between the marginal artery and the bowel was unusually long, and the vasa recta in this part also were unusually long. Some of the vasa recta were displaced by the air cysts, but otherwise showed no abnormalities. There was no abnormal accumulation of the contrast medium in the bowel wall and no arteriovenous shunting.

At a control study 3 months later, the patient was quite well and without symptoms.

Case II. A 66 year old man with severe asthma for several years was referred to the hospital because of hematuria after a blunt trauma against his left flank. Intravenous urography showed a marked reduction of the concentration capacity of the kidneys. A collection of small air bubbles was seen in the left upper abdomen, corresponding to the splenic flexure of the colon. The patient, however, refused further examinations and was discharged from the hospital.

Two years later the patient was re-admitted with a severe anemia. The hemoglobin was 38 per cent (Sahli), the erythrocyte sedimentation rate 128 mm./hour and the creatinine 5.4 mg./100 ml. A large tumor was palpated in the left

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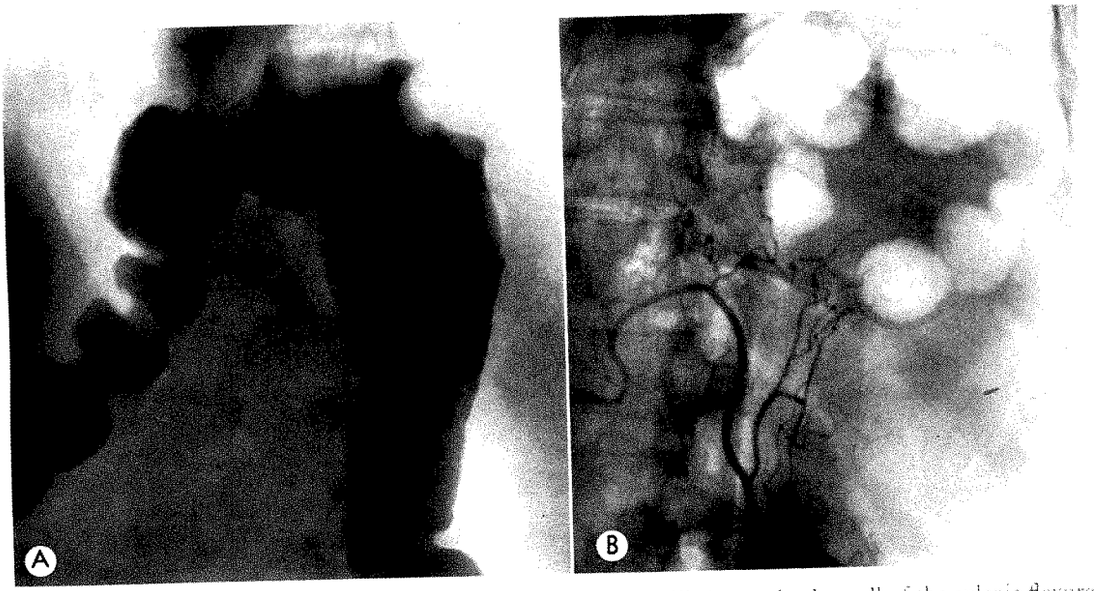


Fig. 1. Case I. (*A*) Barium enema roentgenogram. There are gas-filled cysts in the wall of the splenic flexure of the colon. (*B*) Inferior mesenteric angiogram. The distance between the marginal artery and part of the bowel in the splenic flexure is unusually long. The vasa recta are displaced by the gas-filled cysts.

abdomen and was assumed to be an enlarged spleen. Conventional roentgen examination of the abdomen, however, showed an enlarged left kidney. The right kidney could not be outlined. In the wall of the splenic flexure of the colon small collections of air bubbles were seen. Lumbar aortography showed bilateral enlarged polycystic kidneys supplied by tiny arteries and with very little functioning parenchyma. Inferior mesenteric angiography demonstrated the artery and its branches to be of normal diameter (Fig. 2). In the splenic flexure, where the air cysts were seen in the wall of the colon, the vasa recta did not differ from those in other parts of the bowel examined. No abnormal accumulation of the contrast medium was seen in the wall of the bowel and there was no arteriovenous shunting.

The patient was referred to another hospital for treatment of his kidney disease.

DISCUSSION

According to Koss,[3] pneumatosis cystoides intestinalis is localized to the small bowel in 63 per cent and the colon in 22 per cent of the cases. Less frequently encountered locations are the stomach, the duodenum, the gastrohepatic ligament and the falciform ligament, among others. The cysts, which may be subserosal or submucosal, usually have no connection with each other.

The origin of the cysts is obscure. Patients with pneumatosis cystoides intestinalis seem to have a high incidence of severe asthma[1,4] and duodenal ulcer, often with pyloric stenosis.[3] Keyting *et al.*[2] succeeded in producing intestinal pneumatosis in dogs by injecting air into the root of the

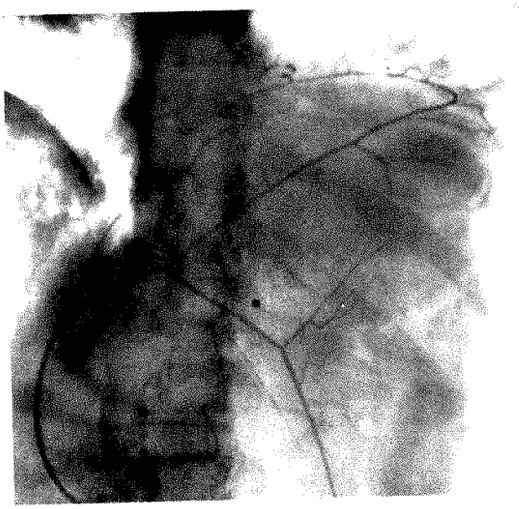


Fig. 2. Case II. Inferior mesenteric angiogram. A large number of gas-filled cysts are seen in the wall of the splenic flexure of the colon. No pathologic changes are demonstrated in the angiogram.

left lung. Bacterial origin of the gas in the cysts has been suggested, but several authors have reported failure to grow organisms from the cysts, and peritonitis does not occur when the cysts rupture.

One of the patients in the present report had severe asthma and polycystic kidneys with renal insufficiency. The other patient had a gallbladder disease. Conventional roentgen examination of the abdomen in one of the patients and colon examination in the other showed typical changes of pneumatosis cystoides intestinalis in the splenic flexure of the colon. Extension of air outside the cysts could not be demonstrated and at angiography no gas was seen to extend along the vessels. The angiography did not reveal any signs of inflammation. The vascularization of the splenic flexure, on the other hand, was sparse, more suggestive of hypovascularization of that part of the bowel in 1 patient. Stenosis or occlusion of the vasa recta was not demonstrated.

The angiography does not contribute to the etiology of the condition, but as the disease is rare any information concerning it is of value.

SUMMARY

Two cases of pneumatosis cystoides intestinalis confined to the splenic flexure of the colon are reported, one with severe asthma and polycystic kidneys, the other with a gallbladder disease.

At angiography of the inferior mesenteric artery, the only abnormality seen was a relatively sparse vascularization of that part of the bowel and displacement of the vasa recta in the bowel wall around the cysts in one of the cases, whereas the angiography in the other case was normal.

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Vol. 117, No. 2

ARTERIOGRAPHIC DIAGNOSIS OF INTUSSUSCEPTION*

THREE CASE REPORTS

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INTUSSUSCEPTION is the term applied to the invagination of one segment of intestine into another. The most useful roentgenographic methods for establishing this diagnosis are plain roentgenograms of the abdomen, barium enema and barium meal examinations, with small intestine study follow-through.[2]

The purpose of this paper is to present the arteriographic findings in 3 cases of intussusception.

REPORT OF CASES

CASE 1. A 37 year old man complained of intermittent abdominal colic at irregular intervals for 6 weeks before his visit to the Outpatient Department on June 25, 1969. An increase in the frequency of bowel movements preceded each attack of pain, and the latter was accompanied by nausea and vomiting. Five days prior to his visit, the pain had increased in severity. The patient described the pain as stretching or pulling in nature. He also passed a reddish-black stool. When examined, he was found to have an irregular, poorly-demarcated mass in a tender area above and to the right of the umbilicus.

On June 25, 1969, an upper gastrointestinal examination (Fig. 1) showed a mass within the duodenal loop causing elevation of the body and antrum of the stomach, plus compression of the third portion of the duodenum. The follow-up roentgenograms of the small intestine (Fig. 2) revealed a long narrow segment involving the terminal ileum, cecum and ascending colon, with marked dilatation of jejunum proximal to the narrowed segment.

Because the location and nature of the disease process was ambiguous, selective superior mesenteric arteriography was performed on July 4, 1969. The arteriograms (Fig. 3, *A* and *B*) showed the right colic, ileocolic and appendicular arteries markedly stretched with their folded branches surrounding a mass. The arterial branches appeared as hairpin-like curves folded transversely and displaced upward into the epigastric region. The involved branches of the right colic artery terminated abruptly in the region of the mass. A tentative diagnosis of ileocolic intussusception was made.



FIG. 1. Case 1. Upper gastrointestinal examination. A mass within the duodenal loop is elevating the body and antrum of the stomach, and compressing the third portion of the duodenum.

To confirm this conclusion, a barium enema examination (Fig. 4) was done. This revealed an obstruction in the midportion of the transverse colon with evidence of intussusception. The ascending colon was not visualized.

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FIG. 2. Case 1. Small intestine. The small intestine is dilated proximal to a long, narrowed segment of terminal ileum.

Exploratory laparotomy showed an ileocecal-colic intussusception complicated by complete intestinal obstruction. The movable cecum and ascending colon, along with the terminal ileum, had been dragged into the transverse colon. After reduction of the intussusception, a fungoid tumor measuring 4×3×3 cm. was found protruding into the lumen of the terminal ileum. About 30 cm. of distal ileum was resected, and ileocecostomy was done. Pathologic examination revealed lymphosarcoma of the terminal ileum, with metastases to adjacent lymph nodes, and ileocecal-colic intussusception.

CASE II. A 44 year old man complained of intermittent episodes of epigastric pain over a period of 1 month. The pain was cutting in nature and subsided spontaneously within a few hours without medication. Three hours before admission on April 14, 1971, he suddenly passed a stool containing fresh blood. When examined, he was found to have a firm, fixed, poorly-demarcated tender mass 5×6×8 cm. in size in the right upper abdomen.

On April 22, 1971, a barium enema examination with air contrast technique (Fig. 5) revealed a mass in the transverse colon near the hepatic flexure, with evidence of intussuscep-

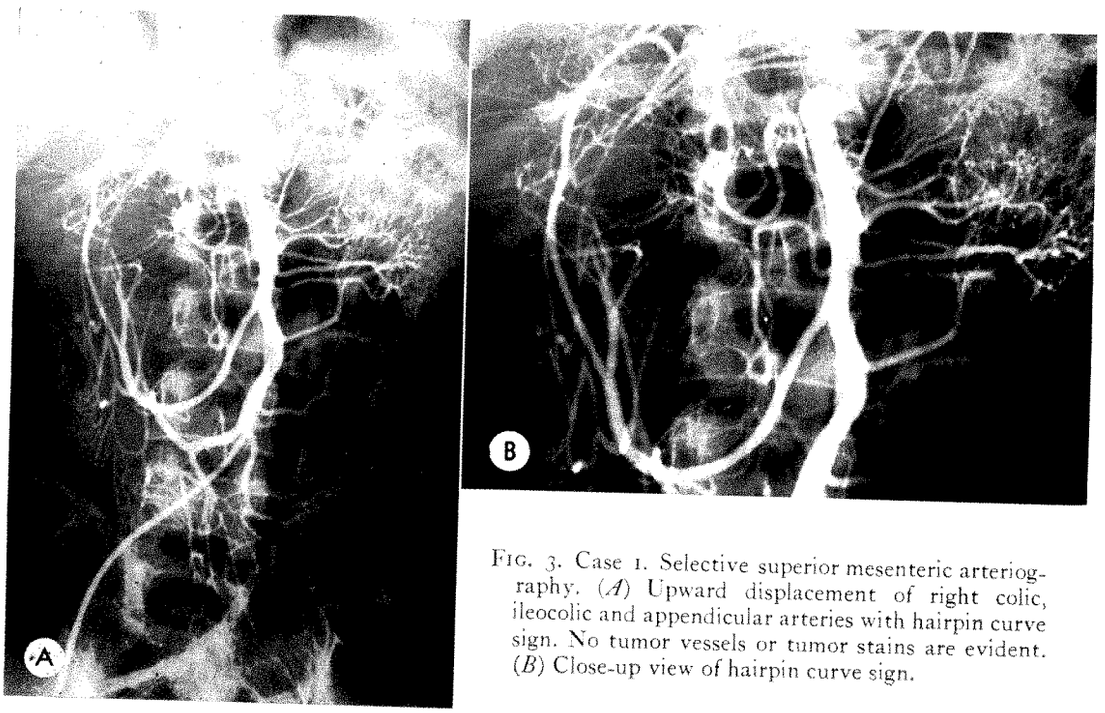


FIG. 3. Case 1. Selective superior mesenteric arteriography. (*A*) Upward displacement of right colic, ileocolic and appendicular arteries with hairpin curve sign. No tumor vessels or tumor stains are evident. (*B*) Close-up view of hairpin curve sign.

tion. Despite manipulation with pressure, the contrast medium did not pass through the mass, and the ascending colon could not be visualized.

On April 23, 1971, selective superior mesenteric arteriography (Fig. 6, *A* and *B*) revealed the superior branch of the ileocolic artery to be dilated and displaced upward, where it anastomosed with the terminal branches of the right colic artery and supplied the mass seen in the barium enema examination. The middle-sized radicles of the superior branch of the ileocolic artery showed the appearance of hairpin curves within the radiolucent center of the mass. The middle colic artery also supplied the mass. The inferior branch of the ileocolic artery and the appendicular arteries were in normal position. A tentative diagnosis was made of tumor of the ascending colon with colon-to-colon intussusception.

Exploratory laparotomy showed an 8×6×5 cm. tumor mass in the hepatic flexure of the colon with evidence of colon-to-colon intussusception. There also were adhesions, edema, congestion of adjacent tissues, and a 4×4 cm. ulceration on the surface of the tumor. A hemicolectomy was performed on the right side. Pathologic examination revealed a mucinous adenocarcinoma of the ascending colon 7 cm. distal to the ileocecal junction, with colon-to-colon intussusception.

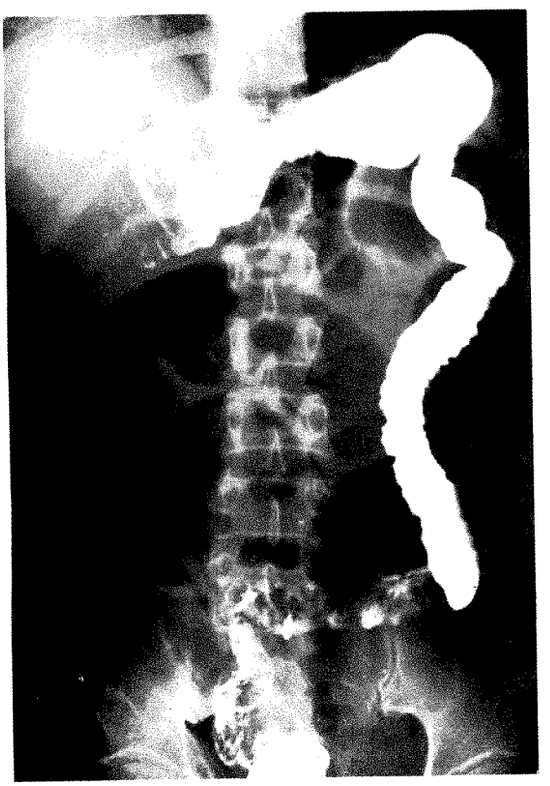


Fig. 4. Case I. Barium enema examination. Intussusception with complete obstruction is present in the transverse colon.

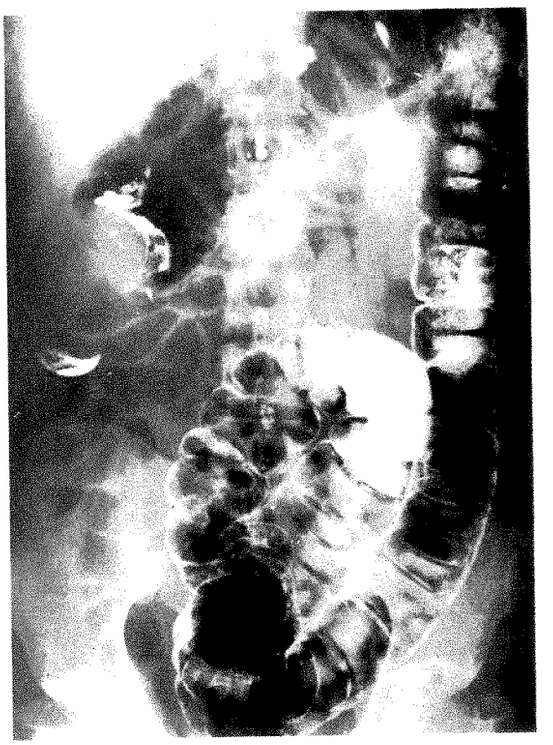


Fig. 5. Case II. Barium enema examination. Double contrast study shows intussusception with complete obstruction in the hepatic flexure of the colon.

Case III. A 59 year old man complained of intermittent periumbilical pain for 1 month. Each attack of pain was preceded by an increase in frequency of defecation. When examined, a sausage-shaped mass was felt in the right lower quadrant of the abdomen.

On October 11, 1970, selective superior mesenteric arteriography (Fig. 7) showed some branches of the ileocolic artery coursing vertically between the normal horizontally directed branches of the ileocolic and right colic arteries. This finding is identical to that described in a patient with ileocolic intussusception by Klein *et al.*[5]

On October 14, 1970, a barium enema exam-

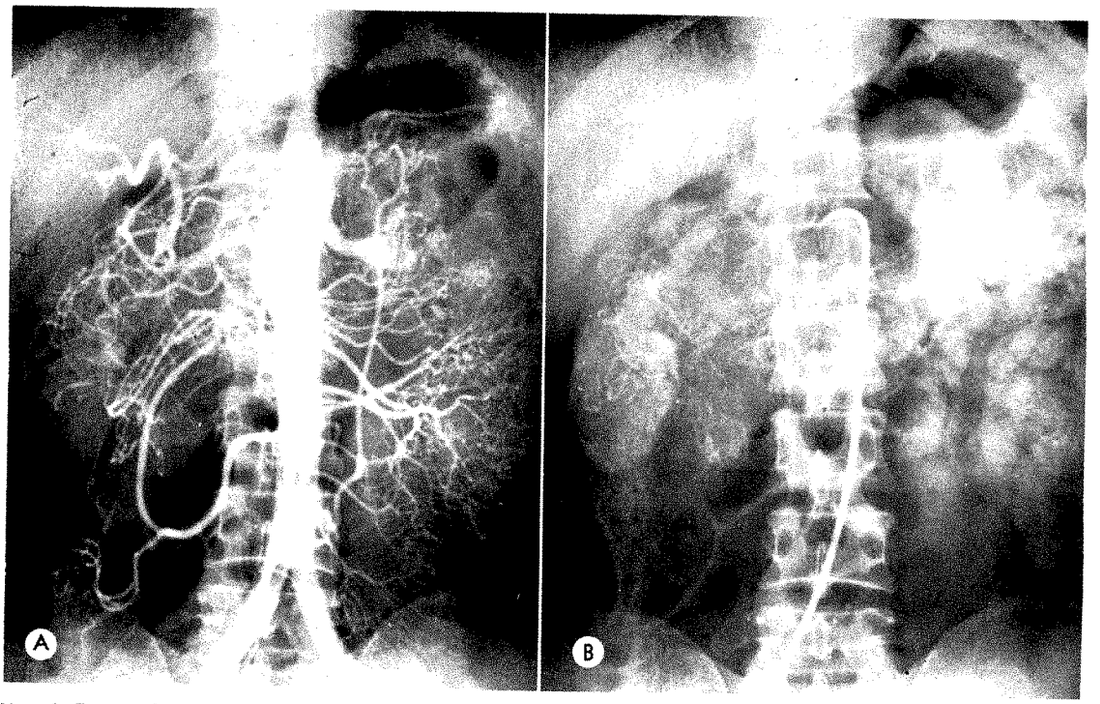


FIG. 6. Case 11. Selective superior mesenteric arteriography. (*A*) There is dilatation and upward displacement of the superior branch of the ileocolic artery, which shows the hairpin curve sign where it anastomoses with the right colic artery. These vessels and the middle colic branches supply a visible mass, but the inferior branches of the ileocolic artery and the appendicular arteries are in normal position, indicating colon-to-colon intussusception. (*B*) Venous phase shows tumor staining.

ination revealed ileocolic intussusception and an abnormal mucosal pattern in the proximal end of the ascending colon.

Exploratory laparotomy showed a marked ileocolic intussusception. After reduction of the intussusception, a firm 6×6×4 cm. tumor mass with a central ulceration was found in the cecum near the ileocecal valve. Several enlarged lymph nodes were noted at the mesocolon near the right colic artery. Right ileocolectomy and ileocolostomy were performed. Pathologic examination revealed a reticulum cell sarcoma of the ileocecal valve with intussusception.

DISCUSSION

Intussusception has been seen at every level of the intestinal tract, from stomach to rectosigmoid.[4] It occurs predominantly in children, since 75 per cent of cases are seen before the age of 2 years, and only 4.5 per cent of cases occur in adults.[2] The most common site of intussusception in children is in the region of the ileocecal valve.[9] The majority of cases in adults are secondary to other diseases. Secondary intussusception usually occurs when an intraluminal neoplasm, either benign or malignant, bulges into the lumen. The tumor then can buckle the wall from which it arises, and both tumor and its attachment are propelled inward into the intestinal tract by peristalsis, thus forming the intussusception.

Roentgenographically, barium enema and small bowel examinations are the most helpful methods for the diagnosis of intussusception.[1] However, selective visceral arteriography also may be used to detect and locate the level of intussusception. Branches of the superior mesenteric artery supplying the intestine normally show a regular distribution.[6] In mild degrees of intussusception, the terminal arterial branches supplying the involved bowel are pulled into the sleeve formed by the intussus-

cepted intestine. This produces a vascular pattern consisting of stretched, parallel vessels closely packed together. These abnormal vessels are displaced from their normal position, and their long axis lies perpendicular to that of adjacent normal mesenteric vessels. As the length of the intussusception increases, larger arterial branches in the mesentery become pulled into the sleeve farther than the bowel which they supply, and these vessels then have to curve backwards in order to reach the bowel wall. This results in the characteristic hairpin curve appearance of the vessels seen in intussusception. The level of the intussusception can be determined by noting which branches of a particular artery are involved. The mass formed by the intussusception may itself be seen as a radiolucent area. If neoplasm is the cause of the intussusception, sometimes the vessels supplying the tumor are detected or tumor staining may occur.

Our first patient had ileocecal-colic intussusception because of a relatively mobile cecum and ascending colon, associated with a tumor of the terminal ileum. In this case, the right colic, ileocolic and appendicular arteries were displaced upward and showed the hairpin curve sign. In Case II, the upward displacement of the superior branch and arterioles of the ileocolic artery also showed the hairpin curve sign, and these vessels supplied the tumor mass. However, the fact that the inferior branch of the ileocolic and appendicular arteries remained in their normal position indicated that the cecum was relatively fixed, and not involved in the intussusception located above. In Case III, the branches of the ileocolic artery ran vertically between the horizontal branches of the ileocolic and right colic arteries, but the absence of the hairpin curve sign indicated a less severe degree of intussusception than in Cases I and II. Absence of tumor staining or visible tumor vessels in Cases I and III may have been the result of either avascular tumors or strangulation of the regional blood vessels supplying the tumors.[7]

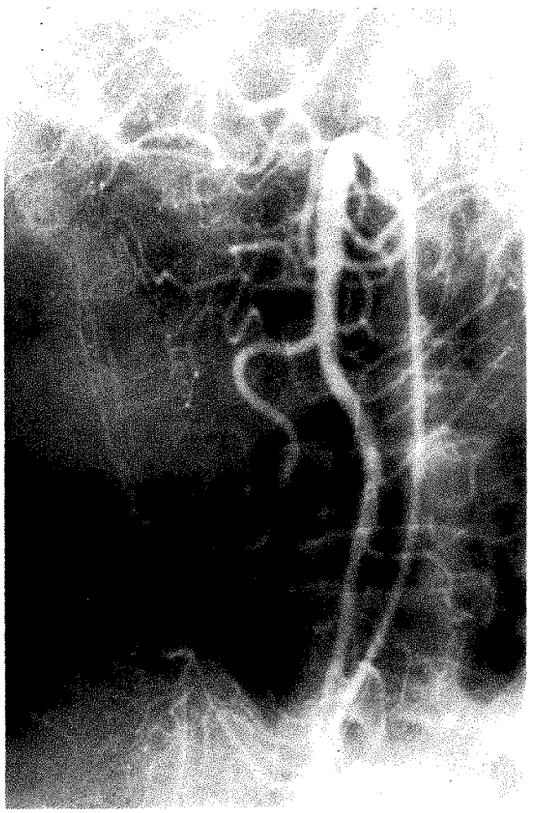


FIG. 7. Case III. Selective superior mesenteric arteriogram. Branches of the ileocolic artery course vertically between the horizontal branches of the right colic artery.

The literature contains reports of peculiar displacement of vessels in superior mesenteric arteriograms. Meyers[8] reported a case of internal (left paraduodenal) hernia, and Bron and Sherman[9] described a case of retroperitoneal hemorrhage with deflection of the branches of the superior mesenteric artery in the upper jejunum, with displacement of bowel loops. However, each different type of lesion may have specific features useful in the differential diagnosis on arteriograms. The changes seen in intussusception are distinct from those caused by simple traction on the branches of the superior mesenteric artery by adhesions alone.[6]

SUMMARY

Three patients with intussusception are described in whom mesenteric arterio-

graphic studies showed changes characteristic of this condition.

The earliest roentgenographic change seen in the arteriogram is a group of stretched, closely packed parallel vessels displaced from their normal position, with their long axis perpendicular to the direction of adjacent normal mesenteric vessels.

In more severe degrees of intussusception, the abnormal vessels become doubled back on themselves, producing the characteristic hairpin curve appearance.

The level of the intussusception can be determined by noting which branches of a particular artery are involved. The mass formed by the intussusception may itself be seen as a radiolucent area. If neoplasm is the cause of the intussusception, vessels supplying the tumor may be identified or tumor staining can occur.

Selective mesenteric arteriography can be a helpful diagnostic procedure when intussusception is suspected.

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Vol. 117, No. 2

MALPOSITION AND DISPLACEMENT OF THE BOWEL IN RENAL AGENESIS AND ECTOPIA: NEW OBSERVATIONS*

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THE purpose of this report is to establish the bowel changes which may be associated with renal agenesis and ectopia. We have observed that specific portions of the intestine may occupy the area of the renal fossa on the side of agenesis or ectopia, or show characteristic displacement and extrinsic mass effect by an ectopic kidney.

These new observations are of clinical importance both in uncovering the renal anomaly and in distinguishing these bowel changes from such conditions as internal hernia, malrotation of the intestines, and displacement by a tumor mass or organomegaly. The associated findings strongly suggest that development of not only the extraperitoneal perirenal fascia, but portions of the intestinal mesenteric fixation, are embryologically dependent upon normal ascent of the kidney.

MATERIAL AND METHOD

The records of 120 patients with the diagnosis of renal agenesis or ectopia seen at The New York Hospital over the 6 year period of 1965–1971 were reviewed. The majority were infants and children without further studies beyond the urologic diagnostic evaluation. Of this group, 11 had both urographic and gastrointestinal contrast studies. Eight of these showed distinctive bowel changes, which in addition to a patient recently encountered at the Mount Sinai Hospital-University of Miami School of Medicine form the basis of the clinical material analyzed.

The anatomic alterations in the extraperitoneal tissues and particularly the perirenal fascial planes accompanying agenesis or ectopic position of the kidney were studied post mortem. A cadaver with a known pelvic kidney was selected and frozen to a solid state by immersion in a tank of dry ice for 36 hours. Horizontal sections of approximately 1½ inch thickness through the abdomen and pelvis were then obtained with a buzz-saw. These were studied, the fascial planes identified and then photographed.

A series of presacral retroperitoneal pneumograms including normal studies and cases of unilateral renal agenesis, pelvic ectopy and crossed renal ectopia were reviewed and analyzed particularly for delineation of extraperitoneal fascia.

ROENTGEN OBSERVATIONS

MALPOSITION OF BOWEL ACCOMPANYING RENAL AGENESIS OR ECTOPIA

On the right side, the descending duodenum may be abnormally positioned posteriorly. Normally, the second portion of the duodenum descends immediately anterior to the medial half of the right kidney. In a right lateral projection during an upper gastrointestinal series, the descending duodenum thus projects anterior to the lumbar spine. With congenital absence or failure of ascent of the right kidney, the descending duodenum may occupy the area of the renal bed and project well over the lumbar spine (Fig. 1*A*; and 2*B*). Its course on a frontal roentgenogram appears normal.

Proximal jejunal loops may also occupy a similar position, filling in the renal fossa and coursing abnormally posteriorly (Fig. 1*B*; and 2, *A* and *B*). At times, their dis-

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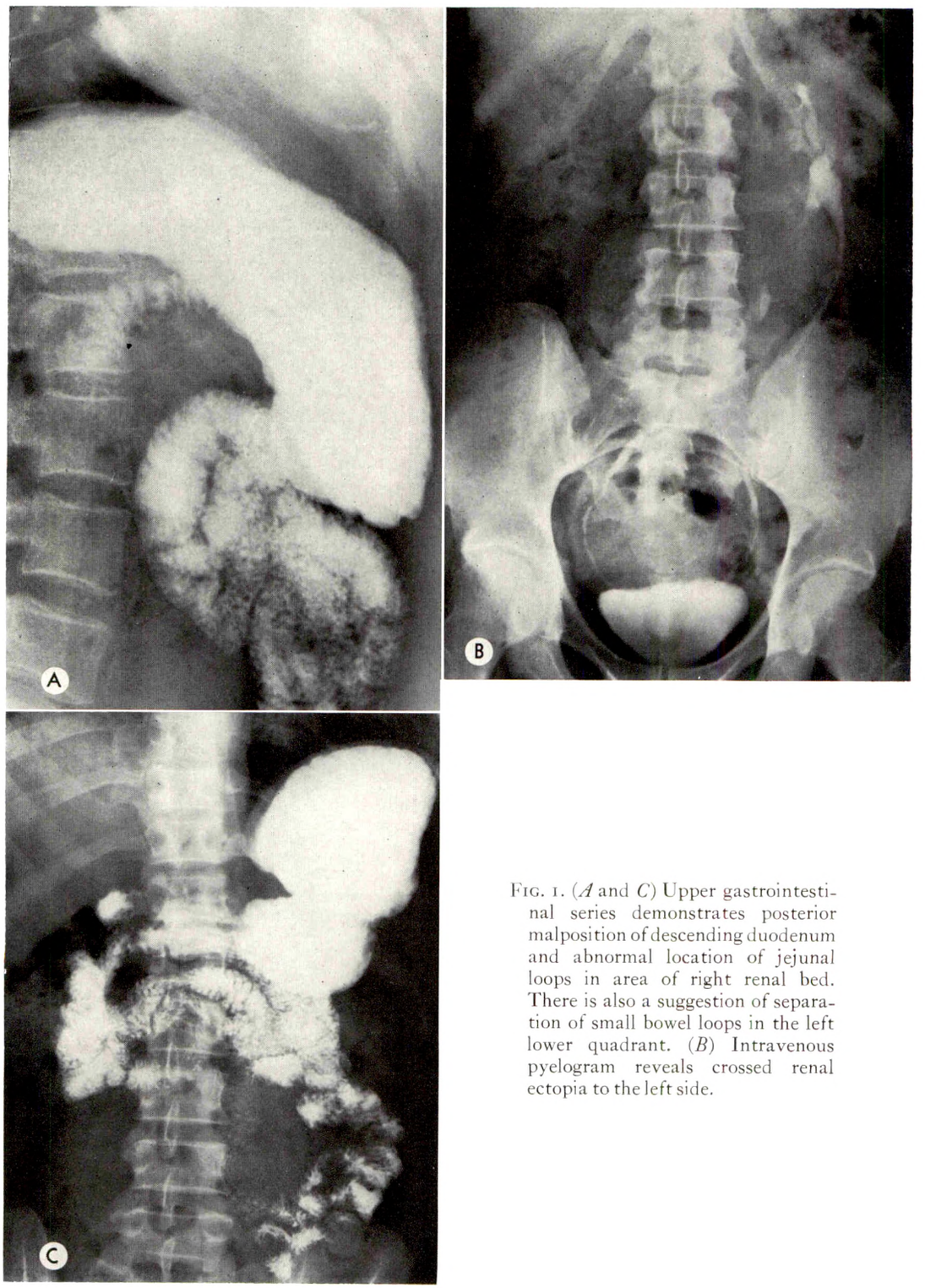


FIG. 1. (*A* and *C*) Upper gastrointestinal series demonstrates posterior malposition of descending duodenum and abnormal location of jejunal loops in area of right renal bed. There is also a suggestion of separation of small bowel loops in the left lower quadrant. (*B*) Intravenous pyelogram reveals crossed renal ectopia to the left side.

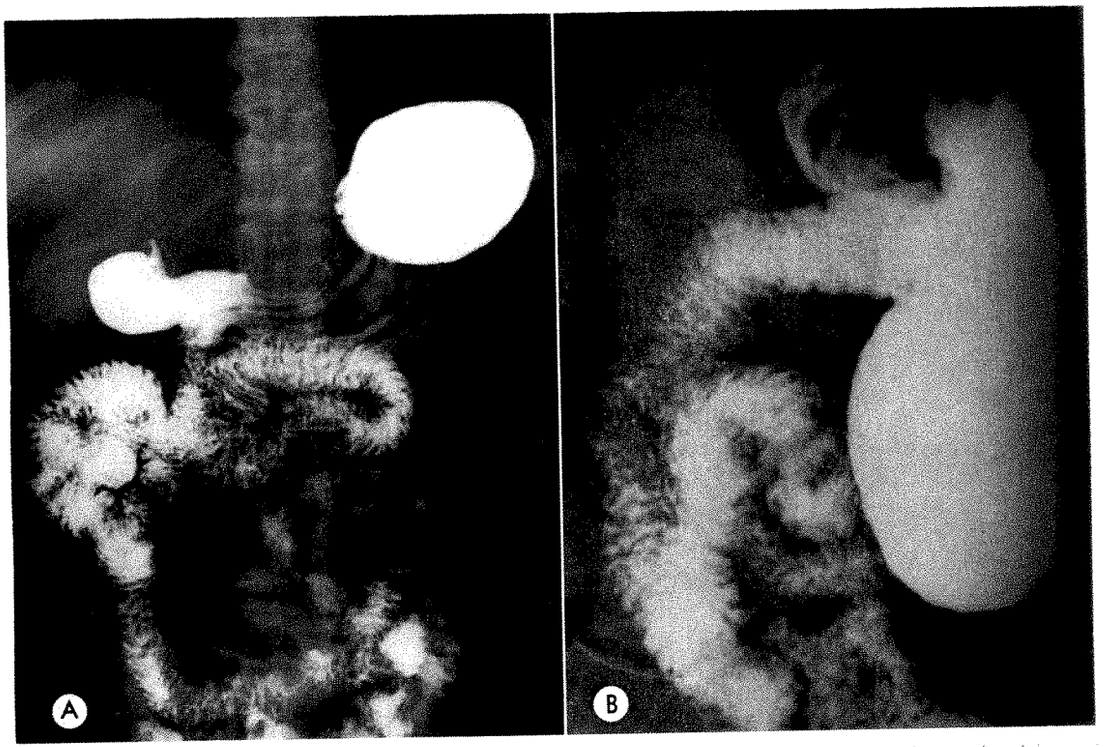


Fig. 2. Case 1. (*A* and *B*) Upper gastrointestinal series demonstrates striking posterior malposition of descending duodenum and proximal jejunal loops, simulating some of the features of a right paraduodenal hernia.

tinctly abnormal position may be confused for a form of internal hernia.

Case 1. Right renal agenesis with intestinal malposition simulating a right paraduodenal hernia.

This 71 year old female was admitted with pain in the right lumbar and sacroiliac areas, radiating from buttock to knee. The pain became worse when walking and was relieved by lying down.

Physical examination revealed slight obesity and mild hypertension. There were no palpable masses or organs. Tenderness was elicited on palpation of the right sacroiliac region. Lumbosacral spine series showed marked degenerative changes at L4-5 and L5-S1.

The patient developed epigastric pain and tenderness, probably secondary to analgesic gastritis. An upper gastrointestinal series revealed posterior malposition of the descending duodenum and proximal jejunal loops in the right flank region (Fig. 2, *A* and *B*). Selective superior mesenteric arteriography showed distribution of jejunal branches in the right upper quadrant with normal origin of the jejunal arteries from the left side of the superior mesenteric artery (Fig. 2, *C* and *D*). Lateral angiographic projections were not performed. Absence of the right kidney and renal artery were noted (Fig. 2, *E* and *F*). However, it was not appreciated that the bowel findings and agenesis of the kidney were related, and a diagnosis of right paraduodenal hernia was made.

At surgery, there was no evidence of an internal hernia. No defect or abnormal fossa could be found in the peritoneum or in the long small bowel mesentery. Following surgery the patient's pain disappeared and on clinical follow-up there was no evidence of gastrointestinal disease.

On the left side, there may be striking posteromedial malposition of the distal transverse colon. Normally, the highest portion of the large intestine in the left upperquadrant("roentgenographic"splenic flexure) retains the mesenteric attachment of the transverse colon. Distal to this, it

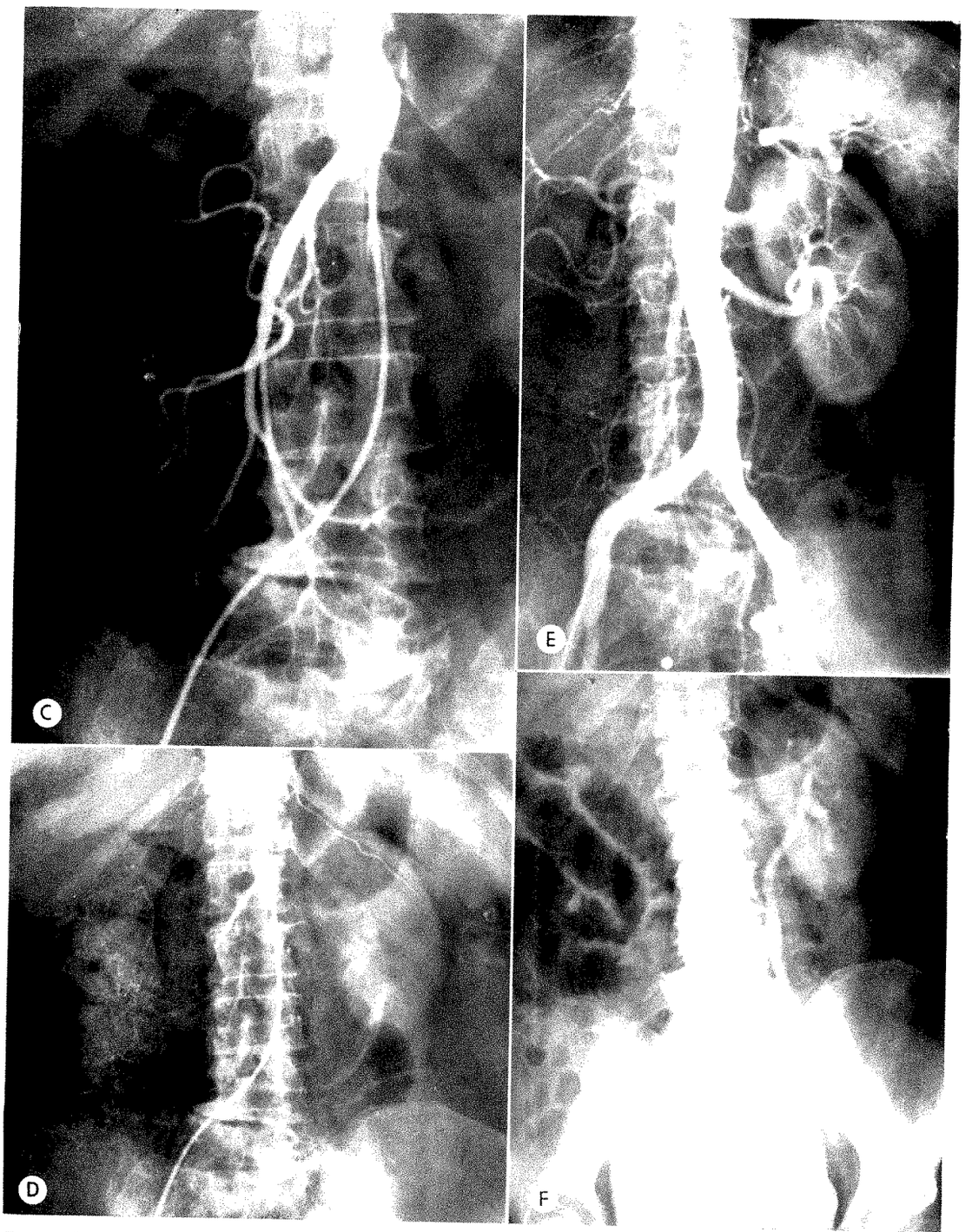


FIG. 2. Case 1. (*C* and *D*) Selective superior mesenteric arteriograms. The arterial phase demonstrates the jejunal arteries arising normally on the left, but then curving to the right mid-abdomen. Note how the capillary blush of the jejunal loops assumes a general reniform contour. (*E*) Flush aortogram and (*F*) delayed roentgenogram reveal absence of the right kidney and renal artery, with compensatory hypertrophy on the left.

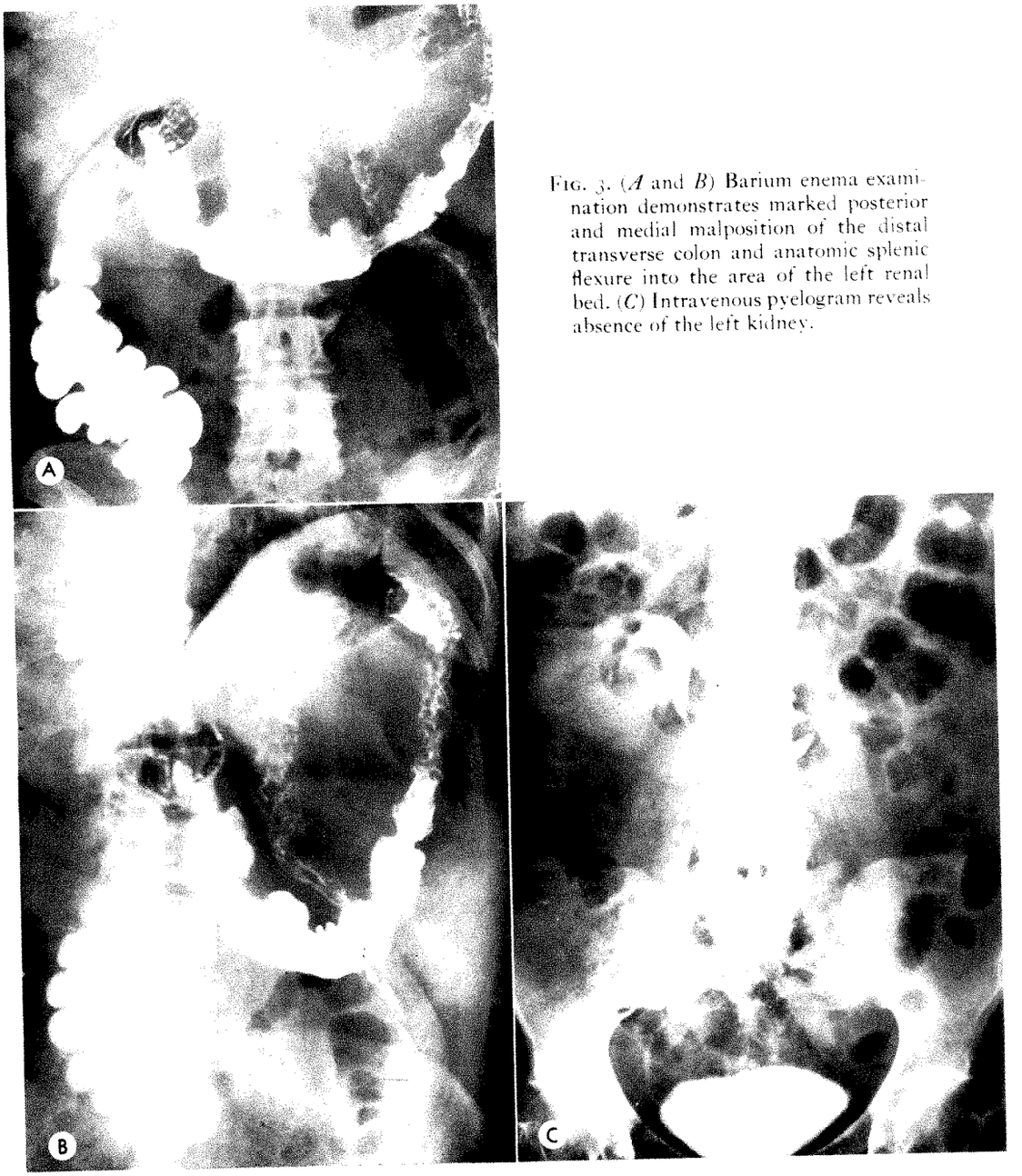


FIG. 3. (*A* and *B*) Barium enema examination demonstrates marked posterior and medial malposition of the distal transverse colon and anatomic splenic flexure into the area of the left renal bed. (*C*) Intravenous pyelogram reveals absence of the left kidney.

courses inferiorly between the medial surface of the spleen and the anterolateral aspect of the left kidney to the "anatomic" splenic flexure in relation to the splenic angle.[17] The anatomic splenic flexure is normally not only the most posterior but also the most fixed portion of the large intestine, being restrained by the phrenicocolic ligament.[13] Distal to this point, the colon continues as the extraperitoneal descending colon.

With agenesis or ectopia of the left kidney, the mesenteric distal transverse colon may be deflected posteriorly and medially into the "empty" renal fossa area. Similarly, the anatomic splenic flexure of the

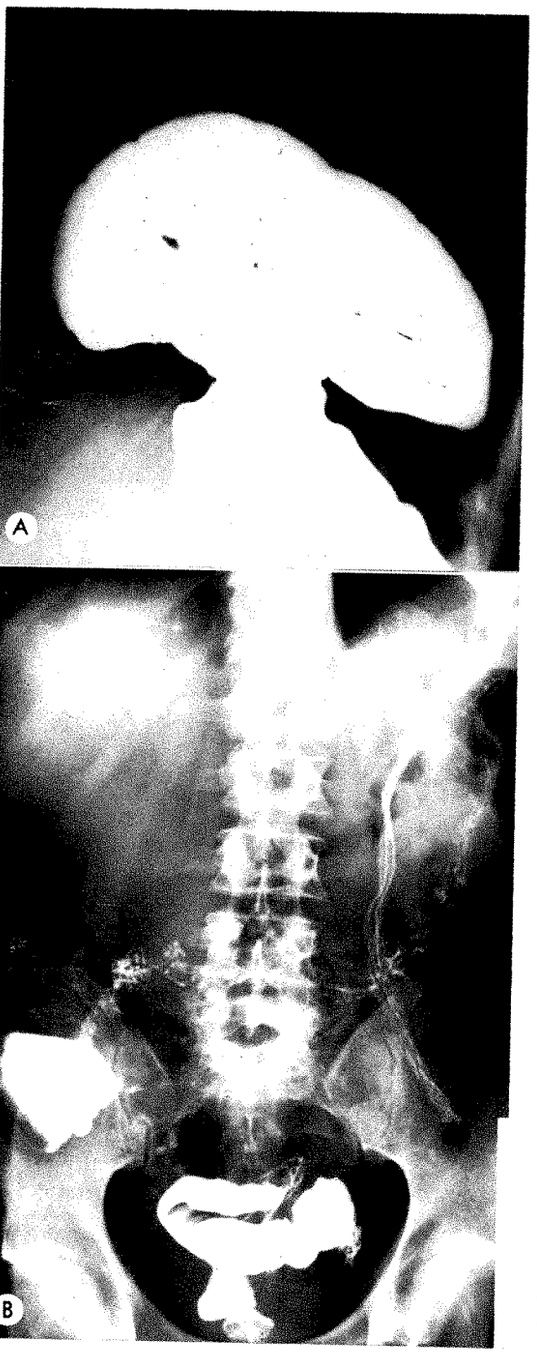


FIG. 4. (*A*) Large intrathoracic diaphragmatic herniation of transverse colon through the foramen of Bochdalek. Lateral view. (*B*) There is also marked medial malposition of the distal transverse colon and anatomic splenic flexure into the area of the left renal bed. These changes are secondary to associated agenesis of the left kidney.

colon may be deflected toward the same site (Fig. 3, *A–C*).

Figure 4, *A* and *B*, illustrates colonic herniation through a large foramen of Bochdalek. Associated left renal agenesis is indicated by the medial malposition of the subdiaphragmatic distal transverse colon and anatomic splenic flexure at the level of the phrenicocolic ligament.

DISPLACEMENT OF BOWEL IN RENAL ECTOPIA

On plain roentgenograms or barium contrast studies, the contour of the density that may be seen in ectopic kidneys usually is not clearly outlined. Two factors appear to account for this: (1) the relative lack of contrasting extraperitoneal fat in the lower abdomen and upper pelvis, and (2) the common marked anterior malrotation of the ectopic kidney. It is the latter feature which also brings the ectopic kidney in the iliac or lower abdominal area into close relationship with the medial borders of the ascending and descending colon and small bowel loops. Failure to recognize the characteristic mass effects and displacements as secondary to renal ectopia may lead to unnecessary surgery.

CASE II. Ectopic kidney presenting as an unidentified mass.

This 24 year old female complained of left lower quadrant pain of a few months' duration. A firm fixed mass was easily palpable. Physical and routine laboratory examinations were otherwise within normal limits. A barium enema study demonstrated an ill-defined mass in the left lower quadrant with pressure upon the medial contour of the iliac portion of the descending colon (Fig. 5*A*). Exploratory laparotomy revealed a left ectopic kidney. A postoperative intravenous pyelogram demonstrated its relationship to the descending colon (Fig. 5*B*).

If displacement of small bowel loops toward the midline can also be demonstrated, the reniform contour of the "mass" may be more clearly shown (Fig. 6, *A* and *B*).

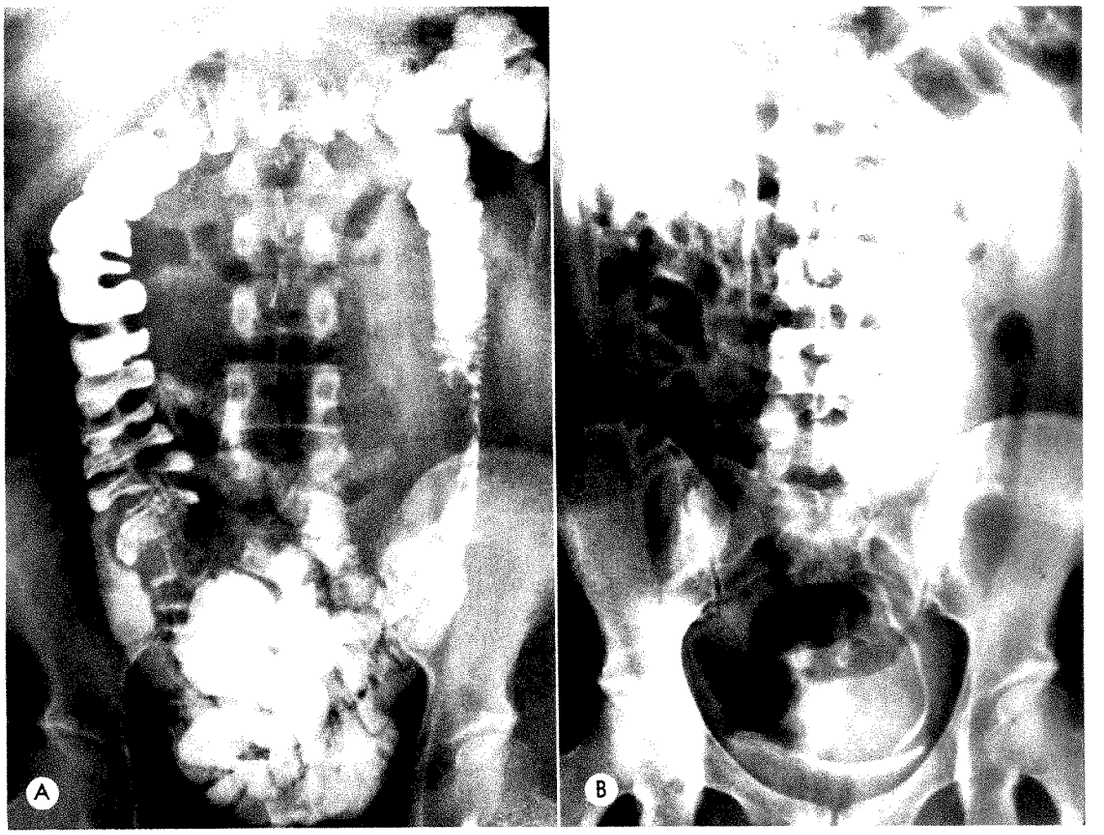


Fig. 5. Case 11. (*A*) Barium enema examination demonstrates extrinsic mass impression upon medial aspect of lower descending colon. (*B*) Intravenous pyelogram documents a left ectopic kidney with marked anterior malrotation in relationship laterally to the descending colon.

DISCUSSION

Ashley and Mostofi[3] believe that the initiating factor in renal agenesis is in the metanephric blastema. Disturbances of embryologic growth from the fourth to the eighth week of fetal life may result in renal ectopia. Normally the kidney reaches its mature level opposite the second lumbar vertebra at the end of the second month. The normal developmental ascent of the kidneys is necessary for the formation of the extraperitoneal perirenal fascial planes.[4,11] With either agenesis or ectopia of the kidney, there is failure of condensation of the extraperitoneal connective tissue in the flanks into well-defined fascial layers. In contrast, the perirenal fascia is present in cases of ptotic kidney. Figure 7 illustrates an anatomic cross-section through an ectopic kidney in the pelvis. While the usual perirenal fascial layers immediately enveloping it are clearly demarcated, these could not be identified in the upper extraperitoneal space on the same side; they were present on the opposite side where the kidney was normally positioned. Similarly, cases of renal agenesis and crossed fused ectopia studied by retroperitoneal pneumography document failure of formation of the perirenal fascia on the side of the absent kidney (Fig. 8; and 9). The lack of restraining fascia appears to contribute to the ease of malposition of bowel into the pliable extraperitoneal fat in the "empty" renal fossa.

It is also apparent from the extreme

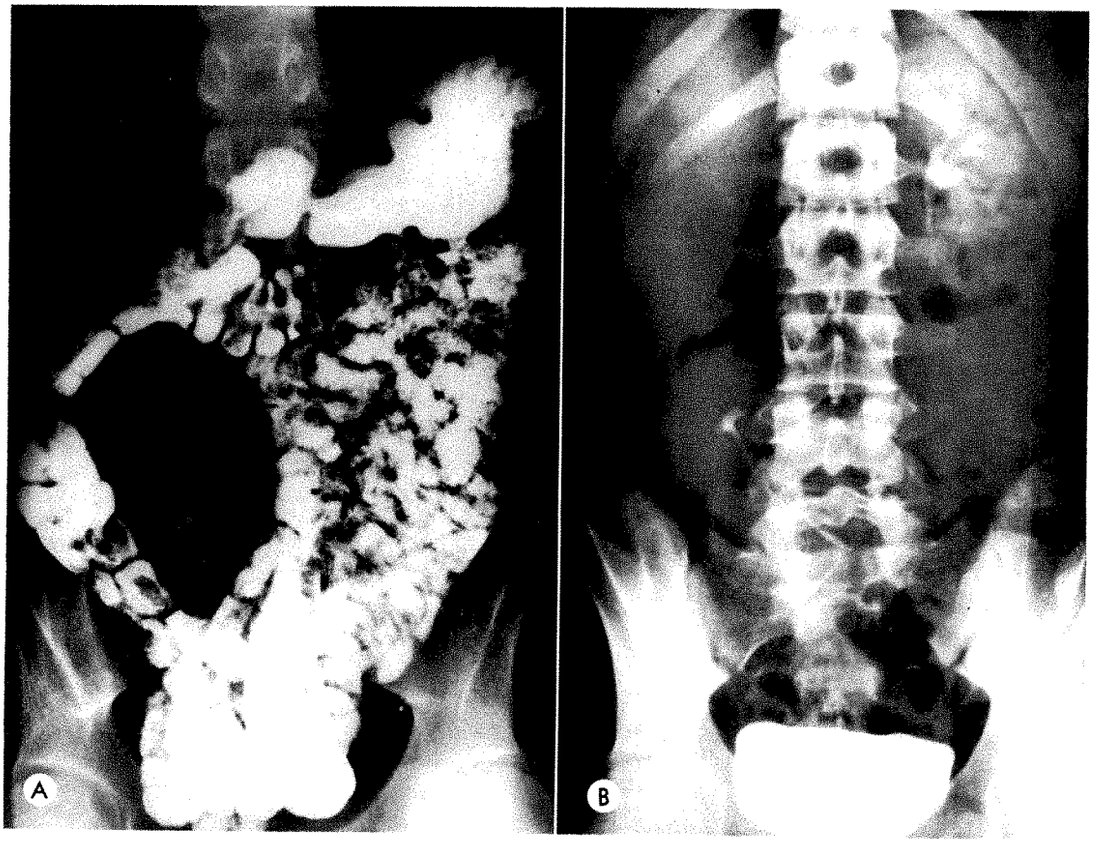


FIG. 6. (*A*) Small bowel series. Inframesocolic mass displacement of the small bowel and colon in the right lower quadrant. Note reniform contour of mass displacement. (*B*) Intravenous pyelogram reveals a lobulated ectopic right kidney with characteristic anterior malrotation.

mobility of jejunal loops and portions of the colon, particularly the anatomic splenic flexure, that there is associated laxity of mesenteric supports of the bowel. Indeed, the phrenicocolic ligament may be absent. The operated case in this series of right renal agenesis with marked malposition of the jejunal loops showed no defects in the small bowel mesentery except for its length.

These changes in intestinal position have not been seen following acquired atrophy or surgical removal of a kidney. Several factors appear to contribute to this—most notably, adipose replacement between the intact perirenal fascial layers or postoperative adhesions in the renal bed, in the face of intact intestinal mesenteric support.

These anomalies are not rare. Unilateral renal agenesis and renal ectopia have been found more frequently on roentgen examination (1 out of 500) than in autopsy series (1 out of 700–1,500).[3,6,8,15,16] The incidence of crossed fused ectopia is only 1 out of 7,500.[1] It has been pointed out that an over-representation may be assumed in urologic cases because pathologic conditions such as stone and hydronephrosis are more common. There is a male to female preponderance in a ratio of 3 to 2, and the anomalies are commoner on the left side.[1,3,4,7,8,14]

The clinical value of these observations is two-fold:

(1) Identification of the characteristic intestinal malposition or displacement on a barium contrast study leads to uncovering of the renal anomaly which may have multiple clinical implications.

The nonspecificity of abdominal symptoms in general and the frequent gastrointestinal symptomatology produced by urinary tract disease[10] often lead to barium

contrast studies as the initial roentgenographic evaluation. Recognition of these bowel changes as being secondary to renal agenesis or ectopia readily leads to the appropriate diagnostic studies.

While such renal anomalies may be compatible with long life, Ashley and Mostofi[3] have pointed out that the incidence of renal disease in a congenitally solitary kidney as a cause of death is, however, high. In unilateral agenesis, the opposite kidney has been found to be diseased in one-third[7] to almost two-thirds[5] of cases, usually secondary to chronic pyelonephritis. Compensatory hypertrophy of the solitary kidney results in a palpable mass in the flank in about 25 per cent.[5] Furthermore, because it projects below the rib cage, it is more susceptible to injury.

In an ectopic kidney or crossed renal ectopia with fusion, the incidence of complications such as lithiasis, infection and hydronephrosis also approaches 50 per cent.[9] Pain in the lower abdomen may lead to such erroneous diagnoses as appendicitis, diverticulitis, neoplasm of the colon, mesenteric cyst, and ovarian disease.

Pelvic ectopy is of obstetric importance because it might complicate delivery. In a review of the subject, Anderson *et al.*[2] concluded that most women with pelvic kidney may be delivered vaginally, but if all the renal tissue lies in the pelvis, as in bilateral ectopy or solitary fused pelvic kidney, the best method of delivery is cesarean section.

Anomalies of structures arising from the urogenital ridge are associated with these renal conditions in as high as 18.5 per cent of cases.[3,7–9] These include vaginal atresia, hypoplastic or unicornuate uterus, and absence of an ovary in females and, less often, monoorchidism and abnormality of the vas deferens in the male. Extragenitourinary tract anomalies are frequently associated with unilateral renal agenesis in children.[7]

(2) Such bowel changes should not be mistaken for a form of internal hernia,



Fig. 7. Anatomic cross-section through pelvis at the level of the iliac crests. An ectopic right kidney (K), deriving its blood supply (arrows) from the lower abdominal aorta, maintains its investment by well-defined extraperitoneal fascial planes (arrowheads). These layers of perirenal fascia are not developed cephalad to the ectopic kidney, where only pliable fat constitutes the extraperitoneal tissues.



FIG. 8. Presacral retroperitoneal pneumography in unilateral left renal agenesis. None of the perirenal fascial layers have developed on the affected side.

abnormality of rotation of the intestines or displacement by a tumor mass or organomegaly. The differential diagnosis of these conditions, while often subtle, is nevertheless clear-cut.

In right renal agenesis or ectopia, the posterior position of jejunal loops within the renal bed might be most readily confused with a right paraduodenal hernia.[12] The loops, however, do not possess the characteristic circular grouping, stasis and dilatation, the identifiable afferent and efferent limbs, or the fixation and nondisplacement within an encapsulated hernial sac despite multiple positions. Distinction is further made by arteriography. In agenesis of the right kidney, jejunal loops and their mesentery and vessels are deflected *anterior* to the superior mesenteric artery into the right flank. In a right paraduodenal hernia, jejunal loops and their mesentery and vessels pass through the fossa of Waldeyer *posterior* to the superior mesenteric artery into a hernial sac of the ascending mesocolon. Frontal projections alone thus show similar findings, with the jejunal arteries arising normally from the left side of the superior mesenteric artery and then coursing abruptly to the right to supply a group of small bowel loops in the right abdomen. Lateral projections during aortography or, more clearly, during selective superior mesenteric arteriography readily differentiates the two.

In left renal agenesis or ectopia, the posteromedial deflection of the distal transverse colon and anatomic splenic flexure into the renal bed should not be confused for displacement by an enlarged spleen. Splenomegaly may depress the anatomic splenic flexure of the colon, but does not displace it medially.

Ectopic kidneys may be located in the true pelvis (63 per cent), in the iliac fossa

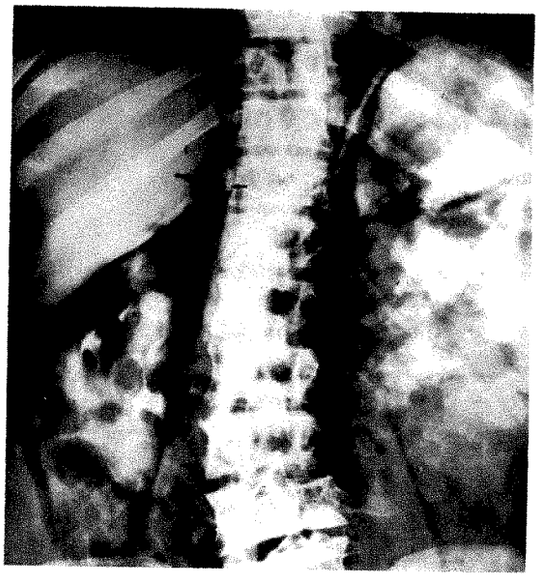


FIG. 9. Presacral retroperitoneal pneumogram with excretory urography in a case of crossed renal ectopia with fusion. While the adrenal glands have normally developed (arrows), there is failure of condensation of the extraperitoneal fat into well-defined connective tissue fascial layers on the side of the absent kidney.

or opposite the crest of the ilium (8 per cent), or in the abdomen below the level of the second or third lumbar vertebra and above the crest of the ilium (29 per cent).[16] In 2 cases of ectopic kidney in the true pelvis studied with barium enema, no definite pressure effect upon the sigmoid colon was noted. This is presumably because the kidney within the sacral hollow does not come into relationship with the anteriorly directed sigmoid loops. The pressure effects of an ectopic kidney in the area of the iliac fossa on the medial aspects of the ascending or descending colon are increased by its malrotation. Simultaneous small bowel displacement may clearly outline the reniform contour of the "mass" (Fig. 6*A*).

CONCLUSIONS AND SUMMARY

Agenesis or ectopia of the kidney is frequently accompanied by characteristic malposition of specific portions of the bowel. On the right, the descending duodenum and proximal jejunal loops and on the left, the distal transverse colon and anatomic splenic flexure may occupy the area of the renal fossa. Renal ectopia, particularly in the iliac fossa or lower abdomen, may result in a characteristic mass effect upon or displacement of the ascending or descending colon.

These observations are of clinical significance both in uncovering the renal anomaly and in distinguishing these bowel changes from such conditions as internal hernia, malrotation of the intestines, and displacement by a tumor mass or organomegaly.

It appears that development of portions of the intestinal mesenteric fixation as well as of the extraperitoneal perirenal fascia are embryologically dependent upon normal ascent of the kidney.

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STARCH GRANULOMATOUS PERITONITIS*

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STARCH granulomatous peritonitis can be elicited by the residual dusting powder on surgeons' gloves, drains, or catheters directly implanted at the time of laparotomy, but has also occurred from starch powder residues introduced into the vagina.[21,24]

It is our purpose to present this entity by reporting 3 additional cases and reviewing the literature with regard to the roentgenologic findings.

REPORT OF CASES

CASE I. J.T. This 20 year old female was readmitted to University Hospitals 2 weeks after an uncomplicated cholecystectomy, because of recurrent right upper quadrant pain which radiated to her shoulder. This was sharp and stabbing in nature, but not associated with anorexia or vomiting. Deep inspiration and the supine position exaggerated the pain. On physical examination, extreme tenderness was evident as well as the suggestion of a deep mass in the region. She was afebrile with a white blood cell count of 10,600 per cubic mm. and a normal differential. An upper gastrointestinal examination demonstrated a subhepatic mass which displaced the distal stomach and proximal duodenum inferiorly and anteriorly (Fig. 1, *A–D*).

The patient's abdomen was then re-explored, at which time the subcutaneous tissues and musculature in the region of the previous cholecystectomy scar were found to be markedly edematous. Multiple adhesions involving several loops of bowel were also present in the subhepatic region, but no abscesses could be found. An enormous number of 3 mm. in diameter peritoneal implants, which were hard and yellow-gray in color, peppered the area. Histologic examination of these as well as the abdominal wall revealed focal granulomata with multinucleated giant cells and other chronic inflammatory cell infiltrations. Refractile foreign material characteristic of starch granules was present within giant cells. No organisms could be found.

Postoperatively the patient was given tetracycline and a short course of prednisone which was completed on the 22nd postoperative day. She became free of pain, although a feeling of tightness persisted. During the succeeding 6 months, however, she noted some mild pain and deep tenderness which was exacerbated by vigorous exercise.

CASE II. D.K. This 55 year old woman underwent abdominal hysterectomy and bilateral salpingo-oophorectomy 6 weeks after internal irradiation for endometrial papillary adenocarcinoma. Her immediate postoperative course was uneventful except for a sterile, serous drainage from the midportion of the incision. This decreased significantly and she was discharged on the tenth postoperative day feeling well. Shortly thereafter, however, she became nauseated, began to vomit, and experienced lower abdominal distention and tenderness. She was admitted to her community hospital, where a white blood cell count of 27,750 per cubic mm. was obtained. Cultures were taken from the yet persistent abdominal wound drainage and a course of ampicillin begun. By the next day the white blood cell count had fallen to 8,750 per cubic mm., but her abdominal distention increased. She was then transferred to University Hospitals.

Upon admission the patient was afebrile and in moderate distress with a distended abdomen. Her pelvis felt indurated. Bowel sounds were absent and the patient denied cramping pain. A plain film abdominal roentgenographic examination showed gas-distended loops of small bowel and ascites (Fig. 2), and a barium examination demonstrated the colon to be patent and not participating in the distention. A portion of distal ileum visualized by reflux was also of normal caliber.

Although the patient became more comfortable, her white blood cell count again rose to a level of 20,700 per cubic mm., despite the fact that she remained afebrile. On the fourth hospital day she suddenly experienced dyspnea associated with a rapid pulse rate and rapidly expired, despite the application of resuscitative measures.

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FIG. 1. Case 1. (*A* and *C*) Precholecystectomy upper gastrointestinal examination. The stomach and duodenum are intrinsically negative and in normal position. (*B* and *D*) Repeat examination obtained 2 weeks postoperatively when the patient had developed recurrent right upper quadrant pain. The gastric antrum and proximal duodenum have been displaced inferiorly and anteriorly by an apparent subhepatic mass.

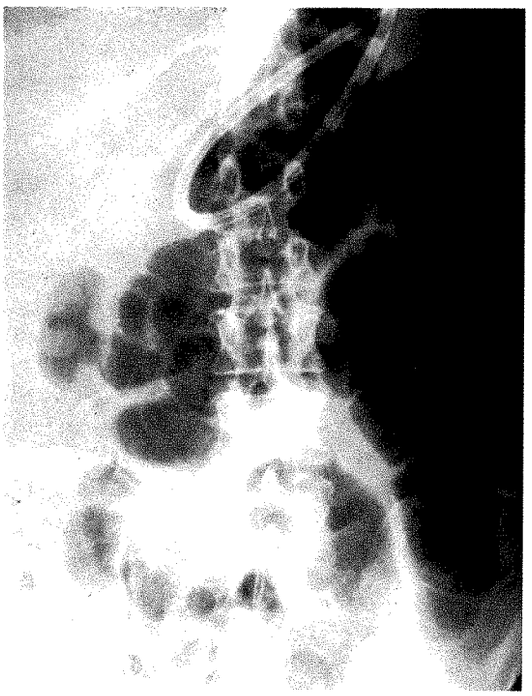


FIG. 2. Case II. Distended loops of small intestine are seen as well as evidence of intraperitoneal fluid.

At postmortem examination a severe granulomatous peritonitis with ascites was encountered. The omentum, mesentery, and bowel walls were thickened and multiple 2 to 5 mm. opacities were present on the peritoneal surfaces; but no mechanically obstructed areas were found. Histologically, giant cell granulomata with eosinophile infiltration were noted in addition to crystals characteristic of corn starch. The lungs were involved in a generalized pulmonary edema without pulmonary or coronary infarctions.

The cause of death was postulated to be the result of a hypersensitivity reaction to corn starch.

CASE III. D.S. This 34 year old man's left inguinal region and retroperitoneum had been explored because of cryptorchism. In the course of surgery the peritoneal cavity was entered. For the first 2 postoperative weeks the patient progressed satisfactorily and was asymptomatic. He then became aware of a left lower quadrant pain which was steady, but accompanied by occasional cramps. Chills, fever, and increasing constipation were perceived. When examined 4 weeks after operation he was not in acute distress, but considerable erythema, induration, and tenderness were present in the region of the healed incisional scar. His temperature was 99.4° F., white blood cell count 6,600 per cubic mm., and 16 lb. of weight had been lost since the prior hospital admission. On a barium enema examination an extramucosal mass which involved the lateral aspect of the distal descending colon was encountered, a site which was directly beneath the incision (Fig. 3, *A* and *B*).

This region of the patient's abdomen was then re-explored. Although no abscess was found, the tissues were edematous and firm

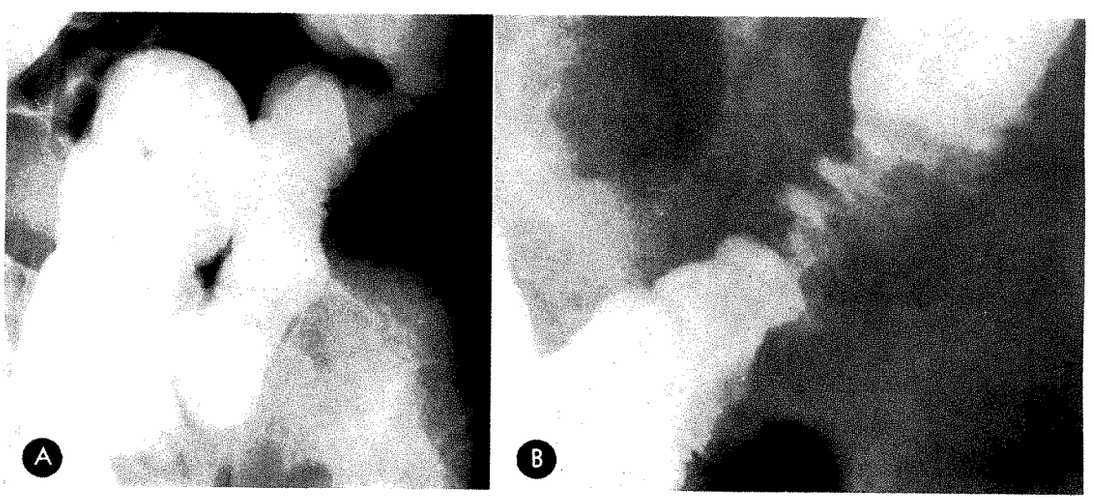


FIG. 3. Case III. (*A*) Barium enema examination. The distal descending colon is displaced medially by a poorly defined mass which has features of being at least extramucosal in origin (*B*).

with granular areas on the peritoneum, but the adjacent colon was free of intrinsic lesions. Multiple biopsies were obtained and the area irrigated and drained. Histologic examinations demonstrated a diffuse chronic inflammatory reaction with numerous focal granulomata and abundant foreign body type giant cells. Although some of these contained PAS-positive material in their cytoplasm, no starch granules were identified. Acid-fast and Grocott (for fungi) stains were negative. The tissue diagnosis was consistent with starch granuloma and no other cause was identified. The interval of 4 weeks was a reasonable time for starch granules to be resorbed.

DISCUSSION

When surgical gloves were first introduced by Halsted, a wet technique was used to lubricate them. This was soon abandoned in favor of a dusting powder that was applied before sterilization. The first agents used consisted of lycopodium spores or a mixture of this with talc (magnesium silicate), thought to be nontoxic. However, in 1933 Antopol[1] reported cases of postoperative granulomata and draining sinuses as a result of both of these agents, although emphasized the harmful effects of the lycopodium. As a result this was abandoned but the talc, which was still considered to be biologically inert by most hospitals, continued to be used as the sole ingredient of the glove dusting powder. Then in 1943 German[7] reported 20 cases of postoperative foreign body granuloma and marked peritoneal tissue reaction induced by talc. Four years later 37 cases of serious complications, including 2 fatalities, were reported by Eiseman *et al.*[6] who stated, "Talc must be banned from the field of surgery."

By this time efforts had been under way to search for an alternative and Lee and Lehman[11] in 1947 suggested a corn starch powder derivative treated to withstand autoclaving. Their animal experiments showed that it was completely absorbed from the peritoneal cavity and had good flow qualities and particle size. The product was subsequently marketed and widely used under the trade name of Bio-Sorb.

The lead author and others,[12] however, later noted some deficiencies in their original experimental protocol and re-evaluated the effect of the starch powder compound in a group of dogs by observing the effect on the peritoneum at multiple time intervals instead of only after an extended fixed period of time, as they had done previously. They found that, although the starch powder was absorbable, it did produce a foreign body reaction as long as it was present. Therefore, if clumps of aggregate particles were present, the reaction would be sustained. They recommended washing gloves prior to surgery.

In 1955 the first cases of starch granulomata in humans were reported.[25] Although the reaction was restricted to incisional areas in these patients, a paper documenting peritoneal involvement appeared the following year.[15] Since then additional reports of starch peritonitis have appeared in the English language literature[2–5,8–9,12,14,16–24,26–29] with the cumulative number of cases being 66 by mid 1972. Included in this group are 2 papers specifically incriminating rice starch,[22,27] which had replaced corn starch in some of the commercial preparations in an attempt to reduce the risks of reaction. The expectation was that the smaller particle size of the rice starch would allow for the use of less powder on the gloves and would be more readily absorbed. The flurry of reports of this complication in recent years has prompted speculation that some alteration in the composition of the starch compounds used has taken place,[19] but there is no evidence as yet to support this.

Considering the ubiquitous use of this material, the incidence of serious complication still remains quite low, although it has been postulated that minor reactions might occur more frequently, being manifest as peritoneal adhesions or transient episodes of postoperative abdominal pain.[28] The possibility of a hypersensitivity reaction has also been suggested (as the pathologist in Case II speculated), but sensitivity tests have been negative,[13,18] except for an atypi-

TABLE I

ROENTGENOGRAPHIC FINDINGS PRIOR TO IDENTIFICATION OF STARCH GRANULOMATOUS PERITONITIS

Total No. of Cases	Roentgenographic Findings not Mentioned	Negative Roentgenographic Findings Indicated	Roentgenographic Findings Described
66	42	7	17 { 14 Distention on plain film roentgenograms; 3 other*

* Cecal filling defect;[9] 1 "partial obstruction of duodenum on upper gastrointestinal examination;[28]" and 1 "lagging right diaphragm."[27]

cal delayed reaction reported in 1 patient.[2] Also, there have been no documented cases of exacerbations, considering that all of the proven cases have been re-exposed to starch at the time of their repeat surgery.[8] Nevertheless, it is apparent that the occasional patient does hyper-react to starch in some idiosyncratic manner.

Previous publications frequently did not mention the roentgenographic findings prior to the identification of the starch granulomatous peritonitis. Those that did, usually described plain film roentgenographic observations of distended loops of small and/or large bowel. None of these cases were illustrated (Table 1). In only 1 instance, where a cecal filling defect was described on a barium examination, was there evidence of a mass. Two of our cases (Cases I and III) did have evidence of extravisceral and extramucosal mass lesions, respectively. These findings were nonspecific as to their etiology and postoperative abscess was considered to be the probable diagnosis in both instances.

The symptoms, which begin approximately 2 weeks after an operation, consist of pain in or around the incision, malaise, and sometimes distention and vomiting. The patients are often afebrile with a normal to slightly elevated white blood cell count. The physical findings consist mainly of tenderness in the area of the incision, which can feel indurated, and/or an ill defined deep mass. Re-operation is usually elected because of the clinical suspicion and inability to exclude conditions such as peritonitis, intestinal obstruction, or abscess. At operation, adhesions, edematous tissues, fluid, and numerous granulomata which seed the peritoneal surfaces are observed.

The histopathologic diagnosis requires the presence of a granulomatous reaction with giant cells and other chronic inflammatory cells including at times eosinophiles. Starch granules should be within the giant cells to exclude those introduced at the time biopsy specimens were obtained. They stain dark blue with Gram's iodine, reddish with periodic acid Schiff (PAS) reagent, and under polarized light are characterized as Maltese crosses 10 to 15 meters in diameter.[2] Identification of the intracellular starch granules provides the definitive diagnosis; however, their absence does not exclude this etiology since they are absorbable. Therefore, if there is a characteristic clinical course, the pathologic findings are compatible, and no other etiology of granulomatous disease can be identified, a strong presumptive diagnosis can be made (Case III).

Postoperatively the symptoms and signs often subside spontaneously after an additional 2 to 4 weeks. There are no documented cases of recurrences.[8] Steroids have been advocated[14] and a short course of treatment seems to hasten recovery, reduce the severity of the symptoms and improve the patient's sense of well being. Prevention, however, is the best remedy and can be accomplished by meticulous cleansing of

surgeons' gloves with wet lap pads followed by rinsing, as well as the continued search for yet a safer lubricating powder.

SUMMARY

The distressful problem of granulomatous peritonitis induced by starch glove dusting powder is discussed; 3 additional cases are reported; and the literature is reviewed as to the roentgenographic manifestations, which are nonspecific for this entity *per se*.

However, when a postoperative patient improves, then, after an interval of approximately 2 weeks, develops pain in and/or beneath the incisional area and has roentgenographic findings of a mass or ileus (paralytic or mechanical), the diagnosis of granulomatous peritonitis should be considered, particularly when he is afebrile or has only mild temperature elevations.

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INTESTINAL CAPILLARIASIS*

A NEW CAUSE OF A MALABSORPTION PATTERN

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IN 1967 an epidemic of severe diarrhea afflicted more than 1,000 natives in the Northern Philippines and resulted in 100 deaths.[1,2] Epidemiologic studies identified the newly discovered species of roundworm, *Capillaria philippinensis*,[4] as the causative agent. Infestation of the small bowel by this parasite resulted in severe derangement of intestinal function which included malabsorption of fats and sugars as well as severe protein and electrolyte losses. A previous description[5] of the small bowel roentgenographic examination of 2 patients with this disease recorded the presence of an abnormal small bowel pattern.

Our experience with an additional 14 patients confirms the presence of a small bowel roentgenographic abnormality and strongly suggests a distinctive malabsorption pattern for intestinal capillariasis.

MATERIAL AND METHOD

Fourteen of the 19 patients with intestinal capillariasis seen at the Philippine General Hospital in 1968–1969 underwent small bowel roentgenologic examinations: 11 males and 3 females were examined; their ages ranged from 10 to 65 years. All patients came from the endemic areas of Ilocos Sur, had laboratory evidence of malabsorption and were found to be passing the *Capillaria philippinensis* eggs in their stool. Marked hypoproteinemia and particularly low serum albumin levels were a uniform finding in these patients. Teenaged boys made up the majority of patients since they were the highest risk group because of their propensity to swim and fish in infected waters. Approximately 18 ounces of U.S.P. barium sulfate were administered by mouth and abdominal roentgenograms were made every hour until the proximal colon was opacified.

ROENTGENOGRAPHIC FINDINGS

All roentgenograms were inspected for the classical signs of the malabsorption syndrome as enumerated by Marshak and Lindner.[10]

1. DILATATION

Any small bowel segment measuring 3 cm. or more in diameter, regardless of its length, was considered dilated: 8 of the 14 patients demonstrated this finding on at least 1 roentgenogram. The dilatation usually involved a short segment and was rarely marked (Fig. 1). The average caliber of the dilated jejunum was 3.4 cm. and of the dilated ileum was 3.6 cm. In general, the same loop of intestine was not consistently dilated from film to film.

2. SEGMENTATION

Isolated loops of bowel distended with barium, maintaining a mucosal fold pattern, and demarcated from adjacent similar units by emptied intervening intestine were considered the criteria for this abnormality. This finding was an uncommon manifestation being present in only 5 patients and marked in but 1. When present, segmentation most commonly was observed in the ileum and was of the delayed variety (Fig. 1).

3. SCATTERING

Also known as fragmentation, this refers to the haphazard distribution of numerous small clumps of barium (resembling snowflakes) in loops of intestine through which the main barium column has already passed. This was the commonest roentgeno-

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graphic abnormality, being present to some degree in all patients examined. In its severest form, very coarse accumulations of barium (Fig. 2) were observed on each roentgenogram in the same patient and eventually in most segments of the small intestine. More characteristic, however, was the presence of a delicate sprinkling of residual barium confined to the middle and distal jejunal and proximal ileal segments (Fig. 3). There was no tendency for the coexistence of segmentation and fragmentation in the same patients, a characteristic noted in other malabsorption syndromes.[10]

4. HYPERSECRETION

The presence of dilute barium (*i.e.*, grayer in color than that proximal to it) and/or flocculation (amorphous large clumps of barium present often in a barium-filled loop) were considered as evidence of increased fluid content. Increased fluid was present in 10 of 14 patients, but in only 1 was it considered to be of moderate extent. More commonly, minimal dilution of barium was present in 1 or 2 loops of small intestine no more than 2 inches long (Fig. 3). This feature was not consistently localized to any one area of the small bowel.



FIG. 1. One hour roentgenogram of a small bowel series in a patient with the severest malabsorption pattern. The proximal jejunum is mildly dilated and has diffusely thickened valvulae conniventes (white arrows). Segmentation and scattering are present in the ileum.



FIG. 2. Coarse scattering of the barium is present throughout the jejunum on this 1 hour roentgenogram of the small bowel series. The segmentation observed in the ileum was followed by similar coarse scattering on the 2 hour roentgenogram.

5. FOLD PATTERN

A precise definition of this abnormality is difficult, because of the wide variations of normals as well as the paucity of objective data of previously described malabsorption patterns. Arbitrarily, thickened



FIG. 3. Scattering of the barium is observed in the distal jejunum as well as in the proximal and distal ileum. The proximal jejunum and the intervening ileal loops are relatively normal except for evidence of a small amount of increased fluid (white arrow) in a short segment of the ileum.



FIG. 4. The valvulae conniventes are abnormal in many areas of the small intestine. Thickening (black arrows) is observed in many segments, while nodularity (white arrows) is present mainly in the mid small bowel.

valvulae conniventes were defined as folds wider than 1.5 mm. Nodularity was considered to be present if the margins of the valvulae conniventes widened from their invariably parallel course over a length of 3 or more millimeters. The mucosal fold pattern was abnormal in all patients, but its severity was never striking. The incidence of valvular thickening predominated over nodularity, the former seen in all patients, while the latter was present in only 5 patients and observed mainly in the distal jejunum and proximal ileum (Fig. 4). Mild valvular thickening, on the other hand, was present throughout at least $\frac{1}{2}$ of the small bowel in 6 of 14 patients (Fig. 4). As has been true of most of the other abnormal roentgenographic features of capillariasis, the findings of valvular thickening were observed most extensively in the distal $\frac{1}{2}$ of the jejunal and proximal ileal areas. This intestinal region is grossly estimated by us to be in the left mid and lower abdomen just above and superimposed over the left iliac wing.

6. MOULAGE

A dilated small intestinal loop in which the fold pattern has been completely effaced leaving a smoothly outlined collection of intraluminal barium defines this abnormality. Only 3 patients evidenced this finding and in each case it was a single short ileal segment which failed to persist on subsequent roentgenograms.

7. TRANSIT TIME

Kim[6] analyzed 315 normal small bowel

studies and found the transit time to range from 15 minutes to 5 hours with a mean of 84 minutes. Using these criteria, no abnormality of motility was present in our patients. No patient opacified the right colon in less than 1 hour and in only 2 patients was the duration as long as 3 hours. The average transit time was 108 minutes.

COMMENTS

In general, in a single patient there was no parallelism in the severity of the abnormalities in any of the 7 roentgenographic features of malabsorption. Note that in Figure 3 there is extensive barium scattering, but this patient had little in the way of mucosal fold distortion. Figure 1 shows the patient whose examination was most abnormal when considering the combination of all the roentgenographic characteristics of malabsorption.

DISCUSSION

Intestinal capillariasis is a severe malabsorption syndrome caused by a small nematode, *Capillaria philippinensis*. This roundworm, measuring 3–4.0 mm. in length and .03–.04 mm. in diameter,[2] was found capable of causing fulminant diarrhea, which in some cases resulted in a mortality rate in untreated males as high as 35 per cent.[7] Common clinical manifestations included vague abdominal pain, hypotension, muscle wasting, edema and death in severe cases in 2 to 4 months.[12] Whalen *et al.*[12] have summarized the clinical and laboratory features demonstrating malabsorption of xylose along with decreased serum levels of carotene, calcium, potassium and proteins.

Extensive epidemiologic studies in the rural areas of Northern Philippines revealed a wide range of primitive eating habits.[2] The inhabitants favor raw and half-cooked foods such as fish, shrimp and crab. These hosts serve as a reservoir for a number of parasites including *Capillaria philippinensis*.

Once ingested, the capillaria egg matures in the human intestine to the adult form.[2] Pathologic findings[3] in autopsied patients reveal the presence of the worm in both the lumen and the superficial layers of the intestine. The most severely affected segment is the jejunum, where large numbers of these parasites may be found in the lamina propria. The histologic alterations include blunting of villi, round cell infiltration and congestion in the mucosal stroma. A recurring life cycle probably occurs within the intestine resulting in self propagation of the infection.[12] It is the documentation of the capillaria egg in the stool which distinguishes the infected, symptomatic patient from the patient in whom the organism exists in a state of commensalism.

Because world travel is becoming commonplace and veterans returning from the Southwest Pacific theatre have been shown to have an increased incidence of intestinal parasitic infections,[1] familiarity with the roentgenologic findings of this newly defined disease is important. While the small bowel pattern in our series of 14 patients showed mild variability in the degree of abnormality (as is true of most diseases resulting in a malabsorption pattern), the tendency to a common group of findings was consistent enough to allow some distinction.

In the only 2 cases of the disease with reported small bowel roentgenograms,[5] prominence of mucosal folds and "puddling" were noted in one and "increased transit time"* in both. All of our patients demonstrated an abnormal mucosal fold pattern, most commonly a uniform thickening of folds which maintained their normal contour. In only 5 patients was the fold pattern distorted enough to be considered nodular. The uniform valvular thickening may, in part, be related to the hypoalbuminemia which was commonly present in patients with this disease. However, the other abnormalities caused by intestinal capillariasis such as nodularity, fragmentation and increased secretions are

* Communication with Dr. O. Sullesta reveals this to mean fast transit time; *i.e.*, less than 1 hour.

not present with intestinal edema[8] and should allow its differentiation. In none of our patients was the transit time abnormal. The time ranged from 1 to 3 hours with an average of 108 minutes.

The most striking and consistent abnormality which occurred in all patients was the scattering of barium. This, as well as other abnormal malabsorption features, most frequently affected the mid small bowel in what was thought to be middle and distal jejunum and proximal ileum. Of interest is that, pathologically, the most severe parasitic infestation and accompanying histologic changes also generally occurred in these areas. This relationship has interesting investigational implication in that perhaps an improved understanding of the mechanics of the radiologic malabsorption pattern would be possible if an animal model with this disease could be developed. It would also allow an objective evaluation of the properties of the multiple commercial barium products now available for a small bowel examination.

U.S.P. barium was the only product available for our study and in considering a differential diagnosis, one must keep in mind that most descriptions of malabsorption patterns are presently based on the use of nonflocculating barium. In spite of this, certain diseases can probably be excluded when the roentgenologic features of capillariasis are encountered. Sprue need not be considered because of its propensity to cause marked intestinal dilatation and excess secretions.[10] Mucosal fold changes are uncommon in sprue. On the other hand, the mucosal fold changes of capillariasis are not as severe as classically described in such small intestine diseases as Whipple's disease, lymphangiectasia or amyloidosis.[10] None of these 3 diseases produces the extensive scattering characteristic of capillariasis.

Perhaps the most difficult and practical differential diagnosis is that of the abnormal small bowel pattern produced by other parasitic infestations. The mucosal fold distortion and increased secretions are more exaggerated in giardiasis. Probably, however, more helpful is the observation that the ileum in giardiasis is spared,[9] whereas in capillariasis the mucosal fold distortion and scattering frequently involve parts or all of the ileum. The absence of roentgenologic changes in the ileum in hookworm and *Strongyloides* would similarly be the observation which would distinguish these diseases from intestinal capillariasis.[9]

Of interest is that in 1961, Middlemis[11] described a malabsorption pattern occurring in the tropics which he labeled idiopathic tropical steatorrhea. The roentgenographic features described are similar to those of capillariasis. This may add some credence to Lindenbaum's[7] speculation that human infestations may have occurred in other parts of the world and gone unrecognized.

SUMMARY

Intestinal capillariasis is a newly described malabsorption syndrome caused by a species of roundworm, *Capillaria philippinensis*.

Roentgenologic examinations of the small intestine performed on 14 patients revealed a consistent malabsorption pattern characterized by scattering of barium and mucosal fold alteration.

The severity and distribution of these and other alterations are discussed and compared to malabsorption patterns caused by other intestinal diseases.

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TUBERCULOUS MESENTERIC LYMPHADENITIS

WITH EMPHASIS ON ANGIOGRAPHIC FINDINGS

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WITH the use of angiography, we provide the surgeon with increasingly more information about some of the more common abdominal masses such as carcinomas and pseudocysts of the pancreas, hepatomas, liver metastases, renal carcinomas, and many others. In a search of the literature, however, we could find no publications describing angiographic findings associated with tuberculous mesenteric lymphadenitis.

We are reporting 2 patients with this entity from the clinical and roentgenologic viewpoints with emphasis on angiographic findings.

ANATOMY

In order to understand tuberculous mesenteric lymphadenitis, we believe that a knowledge of the pertinent anatomy is essential. There are generally 4 chains or groups of lymph nodes that may be involved by tuberculosis retroperitoneally: (1) preaortic; (2) postaortic; (3) right paraaortic; and (4) left paraaortic.

The preaortic chain consists of groups of lymph nodes adjacent to the origins of the celiac, superior mesenteric and inferior mesenteric arteries. These lymph nodes may be involved by tuberculous organisms either selectively or collectively. In addition to attacking these larger groups of lymph nodes, tuberculosis may selectively involve divisions of the larger groups of lymph nodes such as the pancreaticoduodenal group,[7] which lies within the duodenal sweep and is a division of the preaortic chain.

REPORT OF CASES

CASE 1. R. F., 39 year old male, complained of cough and had lost 30–40 pounds over the few months prior to admission. A chest roentgenogram showed cavitating infiltration in the right apex (Fig. 1) suggesting tuberculosis. The diagnosis of tuberculosis was confirmed by laboratory examination.

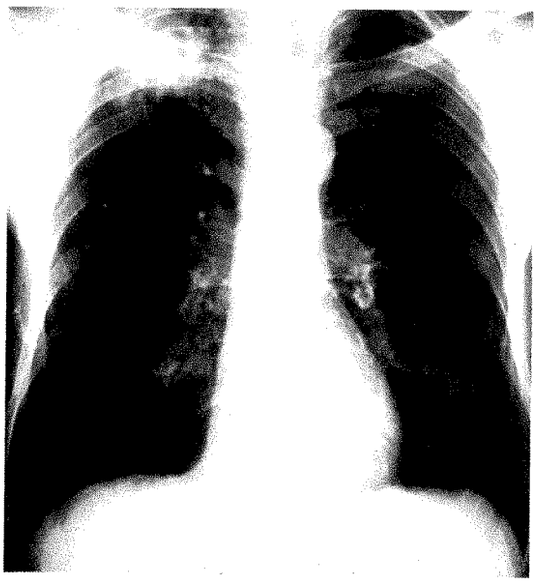


FIG. 1. Case 1. Roentgenogram of the chest shows cavitating infiltration in the right apex.

He also complained of abdominal pain; there was an epigastric mass; and on March 2, 1971, a gastrointestinal series showed compression along the greater and lesser curvatures of the stomach with edema and deformity of the antrum probably because of extrinsic pressure (Fig. 2). Au^{198} liver scan was normal as were two amylase determinations.

The patient was treated with antituberculous drugs (INH, EMB, SM) and steroids.

On March 17, 1971, gastrointestinal series showed persistence of extrinsic pressure on the stomach. The antituberculous therapy was continued but the mass persisted until May 28,

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1971, when we attempted celiac arteriography but were unable to place a catheter in the celiac axis.

We injected the superior mesenteric artery, however, and discovered that extensive collateralization filled the branches of the celiac axis (Fig. 3). We then performed a lateral aortography and found the celiac axis to be stenosed almost to the point of occlusion (Fig. 4, *A* and *B*). Our differential diagnosis was tuberculous mesenteric lymphadenitis, chronic pancreatitis or carcinoma of the pancreas.

It was elected not to operate on the patient. The antituberculous therapy was continued over the next several months and on August 8, 1971, a gastrointestinal series showed no abnormalities (Fig. 5).

On August 19, 1971, we repeated the lateral aortography; the celiac axis was much less stenosed (Fig. 6) and filled via antegrade flow.

The patient had gained weight, felt well and had no mass that we could feel. His discharge diagnoses were pulmonary tuberculosis and tuberculous mesenteric lymphadenitis.

Comment. The preaortic lymph nodes around the celiac axis had apparently been involved and they, in addition to the fibrous adhesions around them, had been large and extensive enough to compress the celiac axis almost to the point of occlusion. As they shrunk and the fibrous adhesions regressed from the medical therapy, the pressure on the celiac axis as well as on the stomach decreased. Because of the lack of histologic proof, one might question the diagnosis of tuberculous mesenteric lymphadenitis in this case and argue that a pseudocyst or chronic pancreatitis caused these problems. With the clinical response the patient had, however, we feel reasonably confident that the abdominal problem was secondary to tuberculous lymphadenitis.



FIG. 2. Case 1. Gastrointestinal roentgenogram made on March 2, 1971, demonstrates deformity of the antrum and duodenum.

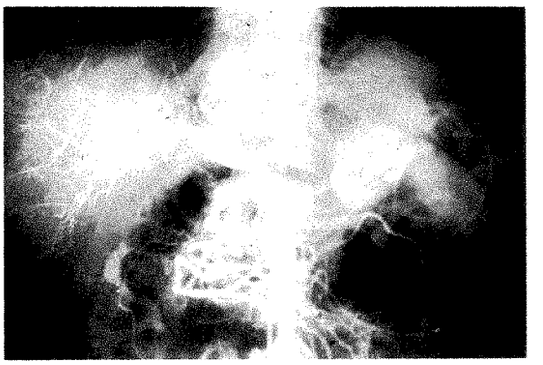


FIG. 3. Case 1. Superior mesenteric arteriogram reveals that the hepatic and splenic arteries fill via retrograde flow through collaterals.

CASE II. T.D., 34 year old male, was treated for syphilis and a slipped capital femoral epiphysis in 1951. He was admitted again in 1955 for a chest mass that was removed. The histology was that of a bronchogenic lymph node with ". . . caseating necrosis compatible with tuberculosis. . . ." No acid fast bacilli were grown from the specimen, however. His PPD skin test was positive at that time. He received no postoperative antituberculous therapy.

He did well until March 1968 when he began to suffer from abdominal pain. A gastrointestinal series showed extrinsic pressure on the duodenum (Fig. 7) probably secondary to the gallbladder. No ulcer was seen, but the patient was treated for peptic ulcer disease. He continued to complain of abdominal pain over the next year. A gastrointestinal series in March 1969 (1 year later) showed severe deformity of the antrum of the stomach and duodenum

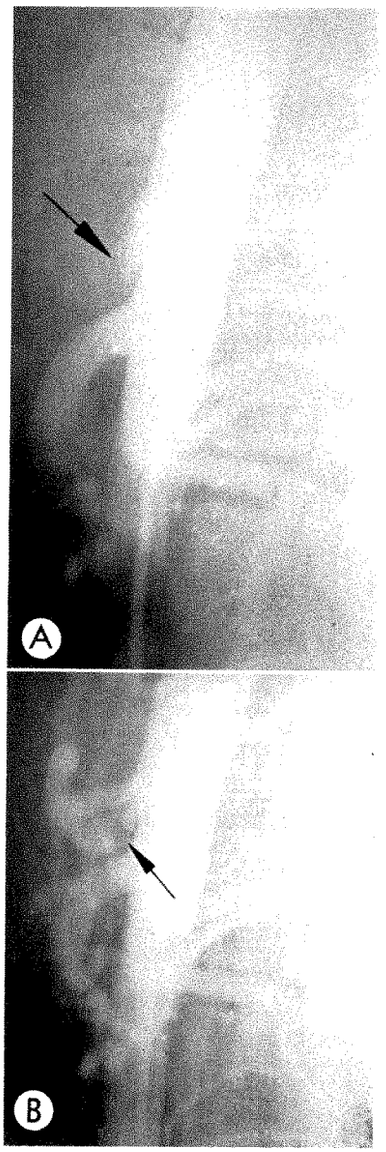


FIG. 4. Case 1. (*A* and *B*) Lateral aortograms. (*A*) Poor filling of a stenosed celiac axis (arrow), with good filling of the superior mesenteric artery. (*B*) Arrow points to stenosis. The celiac axis is filled distal to the stenosis, probably via collateral flow.

(Fig. 8*A*) and a retrogastric mass (Fig. 8*B*). A liver scan showed an abnormal left lobe possibly secondary to an intrinsic mass lesion. He had lost 20 pounds over the 2 months prior to admission and had suffered from chills and fever. A firm, tender, mass to the right of the midline in the epigastrium was felt. A chest roentgenogram was normal except for a deformed 5th rib on the right secondary to the previous thoracotomy (Fig. 9).

A celiac angiogram showed a large, bowed superior pancreaticoduodenal artery with many small branches in the general location of the duodenum and head of the pancreas (Fig. 10*A*). In the capillary phase, there was staining in or around the head of the pancreas or duodenum (Fig. 10*B*). Our impression was either pancreatitis or a carcinoid islet cell tumor of the pancreas. We did not know of the previous operative findings at this time. At peritoneoscopy an abdominal inflammatory mass covered by adhesions was described. The impression was lymph node enlargement or pseudocyst of the pancreas. Two amylase determinations and a barium enema examination were normal.

At abdominal exploration, numerous large matted abdominal lymph nodes extensively involved the lesser omentum, mesentery of the stomach wall and large bowel. A lymph node was opened at the operating table and con-



FIG. 5. Case 1. The gastrointestinal roentgenogram on August 2, 1971, is normal.

tained caseous material; a frozen section was read as granulomatous inflammation. Several other lymph nodes were removed from the stomach wall. The antrum of the stomach, duodenal bulb, and gallbladder were normal to palpation. All the lymph nodes could not be removed, so the abdomen was closed.

On permanent section acid fast bacilli as well as caseating granulomas were present in the lymph nodes.

Antituberculous therapy (myambutal, INH, and streptomycin) was started. The patient took these drugs for 2 years, after which time they were discontinued. He has remained asymptomatic since. No further diagnostic examinations have been performed.

Comment. The filling defect in the left lobe of the liver on the scan was probably secondary to extrinsic pressure from the enlarged lymph nodes. There is no proof of this, however, since no postoperative scanning has been performed.

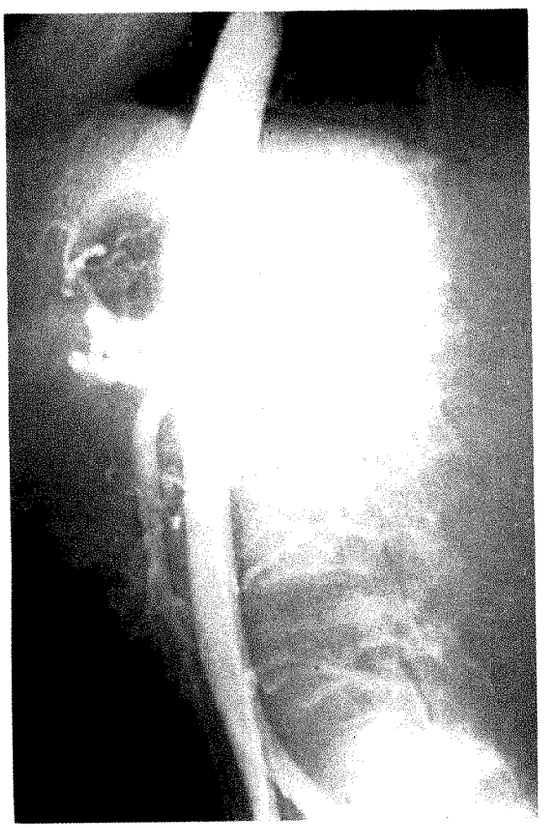


FIG. 6. Case I. Lateral aortogram on August 17, 1971. The celiac axis is less stenosed and filled via antegrade flow.

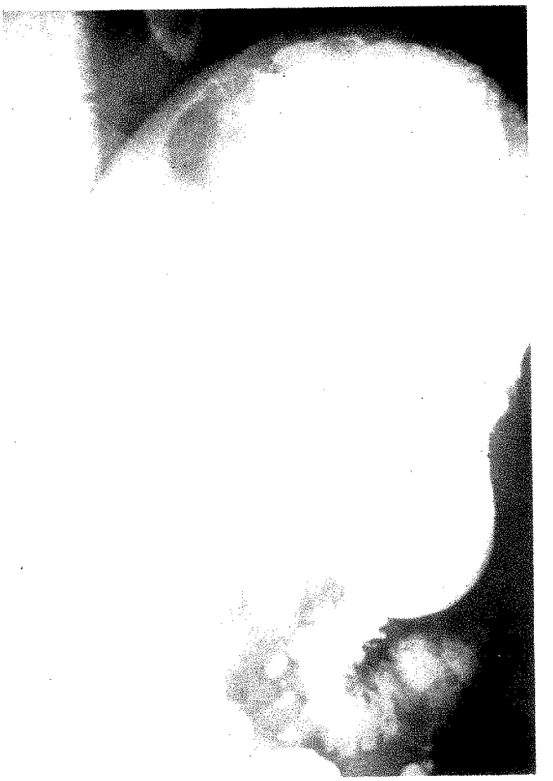


FIG. 7. Case II. The gastrointestinal roentgenogram on March 14, 1968, is normal, except for extrinsic pressure on duodenum, probably from the gallbladder.

DISCUSSION

The age distribution of patients with tuberculous mesenteric lymphadenitis lies between 6 and 55 years. The condition occurs predominantly (73 per cent of the time) in people with pigmented skin.[4] The disease often produces abdominal pain and a palpable abdominal mass. A diagnosis of tuberculous mesenteric lymphadenitis should be considered in patients with abdominal mass even if their chest roentgenogram is normal,[8] as 80 per cent of 55 patients reported by Kent[4] had a negative chest roentgenogram within 2 years of developing tuberculous lymphadenitis. Only 18 per cent of these 55 patients had a history of tuberculosis and only 16 per cent more gave a history of tuberculous contact. Both of our patients were Negroes, 1 had active tuberculosis when we saw him, and 1

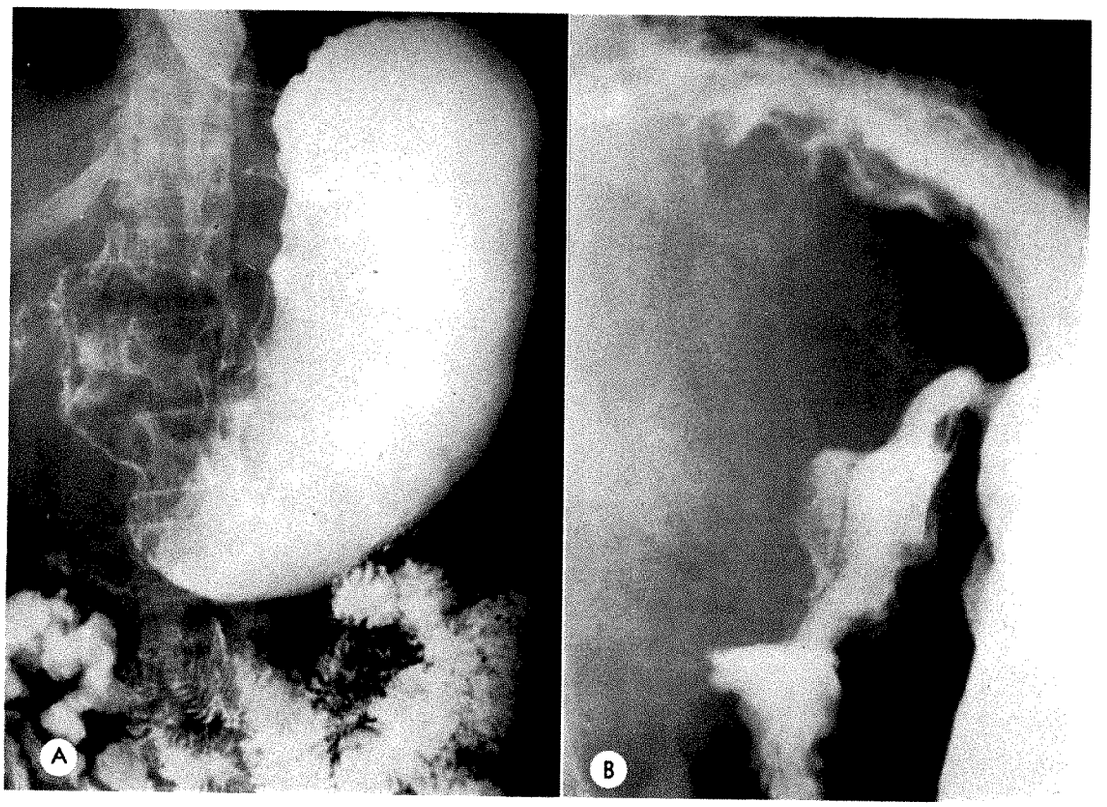


FIG. 8. Case II. Gastrointestinal series in March, 1969. (*A*) Note the irregularity of the stomach and duodenum. (*B*) In lateral view the stomach is displaced anteriorly by a retrogastric mass.

had had a chest lymph node with caseation in it removed 13 years previously. The tuberculosis organisms probably remained dormant in the mesenteric lymph nodes those 13 years and began to grow possibly because of an alteration in the host immune mechanism. This is not an unusual happening, as acid fast organisms may migrate to lymph nodes or to an organ and remain dormant for many years before becoming manifest clinically.[2]

Pathologically, the lymph nodes enlarge, become boggy and produce peripheral fibrous inflammatory changes with adhesions leading to matting of lymph nodes and the production of large conglomerate masses.[6] These enlarged tuberculous lymph nodes may displace the stomach or duodenum, widen the duodenal loop or completely obstruct the duodenum.[3,6,7,9]

In Case I the enlarged lymph nodes, adhesions and fibrous connective tissue reaction on and around the lymph nodes probably encased and narrowed the celiac axis. As the antituberculous therapy shrunk the lymph nodes and caused regression of the fibrous adhesions, the celiac axis became less stenosed. Why the inflammatory response did not involve the superior mesenteric artery is not clear. The preaortic lymph node group was involved in this case, but perhaps not extensively enough to affect the superior mesenteric artery.

In Case II the pancreaticoduodenal group of lymph nodes was most predominantly involved and produced the angiographic findings (*i.e.*, enlargement and bowing of the superior pancreaticoduodenal artery with an increase in the arterial vasculature originating from it). According to the description of the lymph nodes by the surgeon, they probably produced the staining around the duodenum and head of the pancreas (Fig. 10*B*). Other authors have



FIG. 9. Case 11. Roentgenogram of the chest shows only the postoperative changes in the right fifth rib.

described peripancreatic lymph nodes showing staining in the arteriograms;[9] we assume this stain to be due to hypervascularity in the lymph nodes in response to inflammation.

Although none of the findings we have described are specific enough to allow one to make a definitive diagnosis of tuberculous mesenteric lymphadenitis, a knowledge of them would seem to be useful in analyzing the arteriograms of patients with abdominal masses.

Babeau,[1] suggested that lymphangiography is useful in the analysis of patients with tuberculous lymphadenitis. He did not say in his article whether he was able to fill the mesenteric lymph nodes during a leg lymphangiography. We did not perform lymphangiography on our patients. Since in 3 per cent of the cases this disease may be generalized, lymphangiography may be of benefit in assessing the degree of spread.[10] Patients with this disease have been treated with equal success both by having the affected lymph nodes removed from the abdomen or by having them left in and receiving medical therapy.

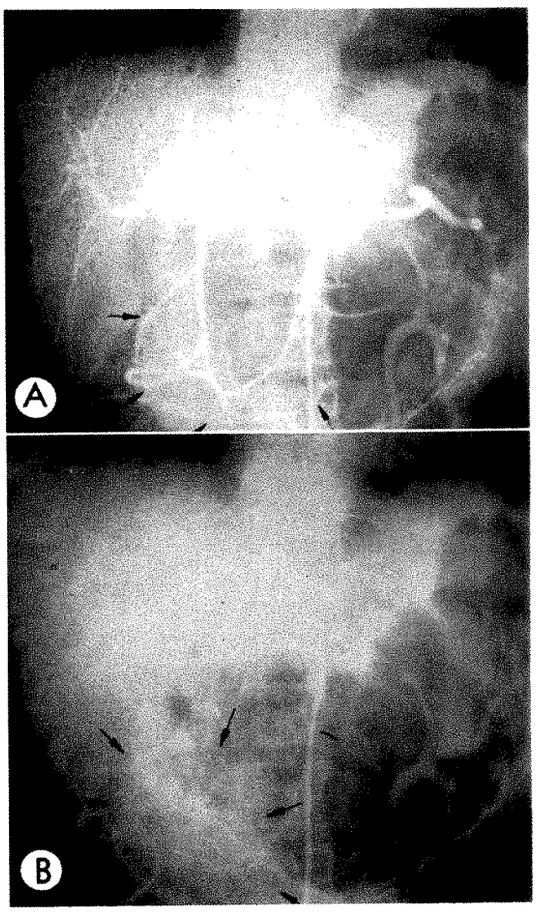


FIG. 10. Case 11. Celiac arteriograms. (*A*) Arterial phase. A superior pancreaticoduodenal artery (arrows) is enlarged, bowed and gives rise to many small branches. (*B*) Capillary phase. Staining is noted in the general location of the pancreas and duodenum, probably in the enlarged lymph nodes found at operation (arrows).

SUMMARY

Two cases of tuberculous mesenteric lymphadenitis with emphasis on the angiographic findings are reported.

In one the celiac axis was stenosed and became less so with antituberculous therapy. The other had enlargement and bowing of a superior pancreaticoduodenal artery and staining around the duodenum and head of the pancreas thought to have been secondary to hypervascularity of the inflamed lymph nodes.

This disease may be successfully treated either medically or surgically.

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PERITONEOGRAPHY*

NORMAL AND PATHOLOGIC ANATOMY

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PLAIN film roentgenographic identification of intraperitoneal structures is generally limited to those aspects outlined by contrasting extraperitoneal fat or naturally occurring intraluminal gas. The demonstration of abdominal masses by gastrointestinal series and barium enema examination requires mucosal alterations or bowel displacement. These routine contrast studies of the alimentary tract permit direct roentgenologic visualization of its internal contour alone. The peritoneal surfaces of the abdominal cavity, the abdominal viscera, and the mesenteries constitute a blind area in radiology. In the roentgen diagnosis of abdominal disease states, those conditions affecting the wall of a viscus, mesenteric attachments, or portions of organs not in contact with structures which may be readily opacified can therefore be only inferred. The peritoneal cavity itself, however, is an opacifiable lumen which is in relation to the external surfaces of bowel, solid organs, peritoneal reflections, and pelvic structures.

Peritoneography consists of double-contrast roentgenologic investigation of the peritoneal cavity and its contents by the introduction of a water-soluble positive contrast medium and gas. While pneumography alone may be helpful for outlining the immediate subdiaphragmatic compartments[2] or pelvic contents,[25,26] it is generally not informative for the remainder of the abdominal cavity. The technique is easily accomplished by the radiologist. No specialized skill or equipment is necessary. The average time required to complete the study is 15 to 20 minutes.

The safety of water-soluble contrast agents in the peritoneal cavity of animals has been established. Histologic study of serosal surfaces and organs has shown either no pathologic changes[16,23,24] or negligible, inconstant and transient inflammatory mesothelial changes.[4,14]

Water-soluble contrast agents have been clinically introduced into the peritoneal cavity of patients in a variety of situations. Their intraperitoneal flow after oral administration has been found useful to document cases of suspected perforated peptic ulcer.[17] Their use in sinography in the determination of peritoneal penetration by abdominal stab wounds is a well established procedure in many institutions.[6,28] They have been employed extensively in large series of patients with neoplastic ascites for the determination of peritoneal loculations prior to the instillation of radioactive material.[12,21] They have also been injected intraperitoneally for the roentgenologic diagnosis of occult inguinal hernias in infants.[8,27,29] In transuterine intraperitoneal transfusions of the fetus for erythroblastosis fetalis, the injection of a water-soluble contrast medium is utilized to ascertain needle placement.[5,9] In none of these instances were local or general toxic reactions observed. Significant features of intraperitoneal structures have been occasionally, but only fortuitously, illustrated. Indeed, it was not until the report of Griscom and co-authors[11] in 1970 that observations in the course of transfusions for severe erythroblastosis fetalis were made regarding the internal roentgenographic anatomy of the intrauterine fetus.

The use of supramesocolic injections of water-soluble contrast agent into the

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peritoneal cavity of a limited number of normal human subjects by Bétoulières and co-authors[3] in 1961 first indicated the clinical possibility of peritoneography. Its diagnostic applicability was further encouraged by the excellent experimental investigations of Margulis *et al.*[15] In a group of animals, simulated tumors attached to the liver, stomach and pelvic wall could not be appreciated by conventional intraluminal contrast studies of the bowel, but were easily identified by positive contrast peritoneography. Air alone was found to be a poor contrast medium. Detailed histologic study confirmed the safety of the procedure. Gelfand[10] applied the method of high volume positive contrast peritoneography in cadavers and visualized many anatomic structures.

The purposes of this report are multiple: (1) to describe the technique of peritoneography and show its safety and feasibility as a diagnostic procedure; (2) to introduce and document *in vivo* the extent of visualization of intraperitoneal structures not conventionally identifiable; (3) to demonstrate the *presence* of intraabdominal disease not shown otherwise; (4) to outline the *extent* of intraabdominal disease, not realized by conventional methods; and (5) to contrast the degree of visualization of the peritoneal contents by peritoneography and peritoneoscopy.

Basic to the appreciation of pathologic alterations is a knowledge of the peritoneographic appearance of normal structures. Since these are often related to mesenteric attachments which are ordinarily not within the framework of orientation of the radiologist, anatomic drawings are used in this presentation to accompany the roentgenographic illustrations.

MATERIAL AND METHOD

The study was performed in 26 hospitalized patients ranging in age from 28 to 74 years, and was comprised of 16 males and 10 females.

A laxative is administered the night before the examination. No premedication is required. Following a cleansing enema and emptying of the bladder, the patient is positioned supine on the radiographic table and a preliminary roentgenogram is made. After local anesthesia, transabdominal puncture is made in the left supraumbilical area lateral to the border of the left rectus abdominis muscle using a Rochester needle* directed with slight medial obliquity. After the needle is introduced into the peritoneal cavity, negative pressure is applied to the syringe, to check for possible puncture of the bowel, bladder, or a blood vessel. These potential complications, however, are largely theoretic and are rarely hazardous in practice.[25] The inner metallic needle is then withdrawn, leaving the flexible plastic outer cannula *in situ*. A 17 gauge needle, either $2\frac{1}{2}$ or $4\frac{1}{2}$ inches long depending upon the thickness of the abdominal wall, is used. Under fluoroscopic control a small amount of air or meglumine diatrizoate† may be injected to document that the needle is in the peritoneal cavity. The needle is then connected by a one-way stopcock and tubing to the nitrous oxide tank. An anesthesia machine with a short-circuited rebreathing mechanism provides a ready source of nitrous oxide. Approximately 1,200–1,500 ml. gas is introduced over several minutes into the peritoneal cavity.

With moderate distention of the abdomen produced, the needle is disconnected from the gas-supply apparatus and 150 to 200 ml. of 60 per cent meglumine diatrizoate diluted with 50 to 75 ml. of normal saline is instilled into the abdominal cavity. A test dose of a few ml. is first introduced and the patient observed for adverse reactions. An open intravenous drip is maintained throughout the study and the vital signs monitored. Adequate antihypersensitivity medications are accessible. An obturator or plug is then inserted into the cannula, and the plugged

* Jelco Intravenous Placement Unit, Jelco Laboratories, Raritan, N. J.

† Renografin 60, E. R. Squibb & Sons, New York.

end taped to the skin to prevent dislodgement. Roentgenograms of the abdomen are then obtained in various positions, supplemented by image-amplified fluoroscopic observations. In several patients of the study, fluoroscopy together with abdominal roentgenograms were obtained after successive increments of 50 to 75 cc. of the contrast medium solution were directed into various intraperitoneal compartments.

Following the roentgenologic examination, the plastic cannula is opened to permit the gas to escape. After as much nitrous oxide as possible has been expressed from the abdomen, the cannula is removed and the puncture site covered with a small sterile dressing. The patient remains recumbent for about 30 minutes to 1 hour to allow further absorption of the gas and to minimize abdominal distress and referred shoulder pain on assuming the upright position.

In 2 patients, a simultaneous upper gastrointestinal series with barium sulfate, and in a third, a timed intravenous cholangiography were performed.

The technique can be easily modified to accompany direct visualization by peritoneoscopy. This procedure requires preliminary sedation and is most commonly done in the operating room or endoscopic suite, but can be performed in the Department of Radiology under proper sterile precautions. It requires a small incision at the same needle site following the introduction of the gas to facilitate controlled peritoneal penetration by the instrument. The renografin solution can thereafter be instilled directly *via* the peritoneoscope. After the instrument is removed, with as much gas as possible retained, the incision is sutured and roentgenograms are made.

FINDINGS

A survey appraisal of the peritoneal cavity (Fig. 1, *A* and *B*) can be obtained or selective compartments and structures can be preferentially visualized by positioning. The entire parietal and virtually all of the visceral surfaces of the greater

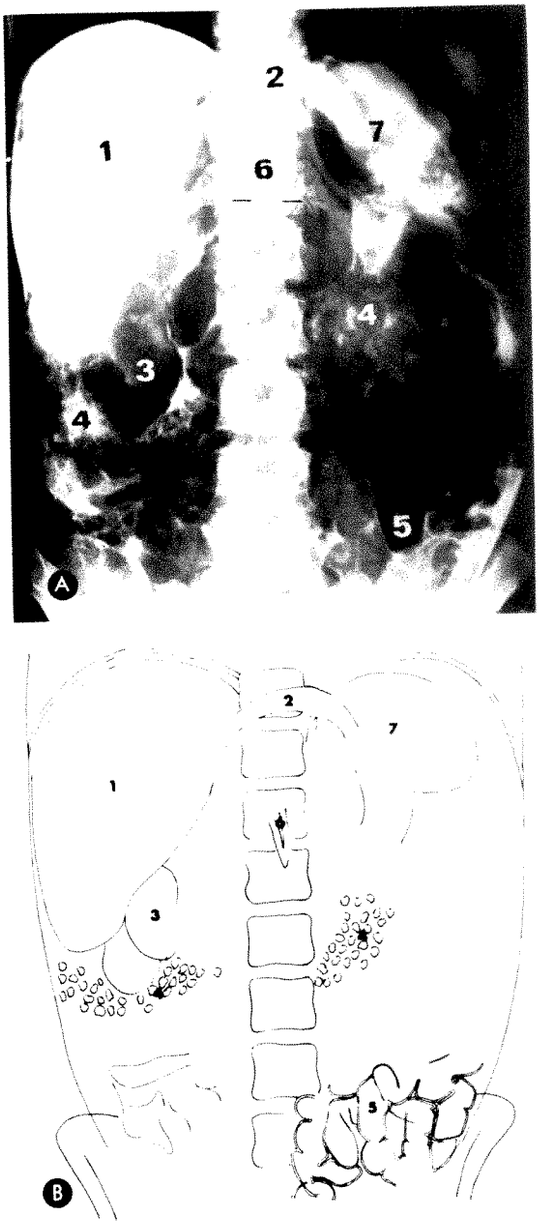


Fig. 1. (*A* and *B*) Prone peritoneography. (1) Positive contrast medium coats the ventral surface of the right lobe of the liver. (2) The arcuate collection resides within the median subphrenic space, anterior to the stomach beneath the central tendinous portion of the diaphragm. (3) The gallbladder displaces the positive contrast medium and is outlined as a "filling defect." (4) The greater omentum presents a characteristic honey-combed appearance. (5) The walls of bowel loops are outlined by contrast medium in the peritoneal cavity and intraluminal gas. (6) The falciform ligament. (7) The spleen.

TABLE I

STRUCTURES ROUTINELY VISUALIZED BY PERITONEOGRAPHY

Organs
- Liver
  - Right lobe—entire peritoneal surface
  - Left lobe—anterior surface
- Gallbladder
- Spleen
- Tail of pancreas
- Stomach
- Bowel loops
- Dome of urinary bladder
- Uterus
- Ovaries

Peritoneal Reflections and Ligaments
- Parietal peritoneum
- Greater omentum
- Lesser omentum
- Transverse mesocolon
- Ligaments
  - Coronary (triangular)
  - Falciform
  - Lienorenal
  - Gastrolienal
  - Phrenicocolic
  - Umbilical

peritoneal sac can be shown. No contrast medium gains entrance to the lesser sac (omental bursa). Table 1 shows the abdominal structures which are routinely visualized. Peritoneography allows the roentgenographic visualization and determination of: (1) external surfaces and contours of abdominal organs; (2) peritoneal reflections and recesses, serosal surfaces and mesenteric attachments; and (3) the thickness of the wall of portions of the alimentary tract.

Figure 2 illustrates that the right lobe of the liver is suspended within the greater peritoneal cavity by its supporting ligaments. The right lobe of the liver is the most conspicuous structure in the abdominal cavity seen during peritoneography, which permits visualization of not only its parietal contour but its deep visceral surface as well, up to its bare area at the reflections of the coronary ligaments (Fig. 3). While an old inflammatory process may leave residual adhesions, demonstrated patency of the perihepatic peritoneal spaces (Fig. 3) was useful in this series in excluding a clinically suspected subphrenic or subhepatic abscess.

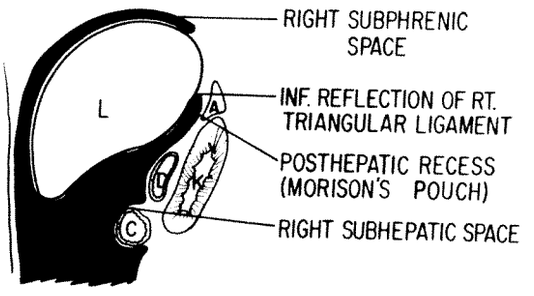


FIG. 2. Diagram of right paramedian sagittal section. The right subphrenic and subhepatic spaces are continuous. Opacification of these peritoneal recesses permits evaluation of the contours of the right lobe of the liver. L-Liver; K-Kidney; A-Adrenal gland; D-Descending duodenum; C-Transverse colon.

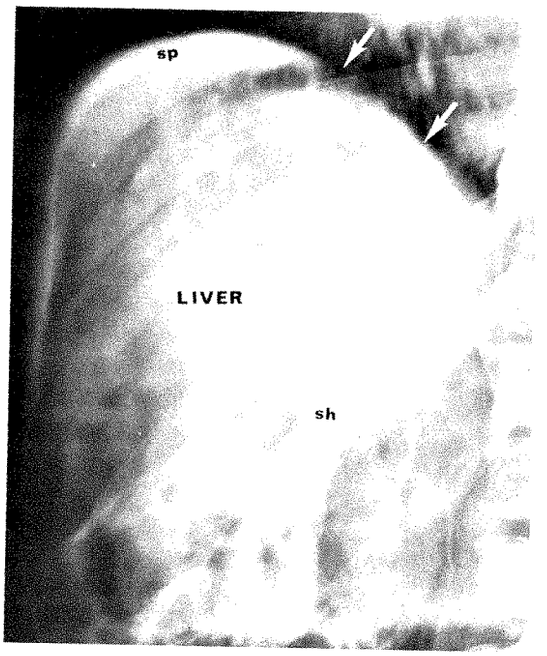


FIG. 3. Peritoneography. Right posterior oblique (RPO) Trendelenburg position. Positive contrast medium extends up both the right subhepatic (sh) and subphrenic (sp) space to the reflections of the coronary ligaments posteriorly at the bare area of the liver (arrows). The entire peritoneal surface of the right lobe of the liver is visualized. Compare to Figure 2. Patency of the perihepatic spaces excludes an inflammatory process. There is some excretion by the kidneys.

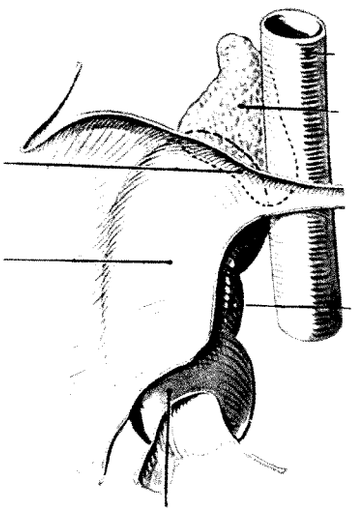


FIG. 4. The anatomic relationships of Morison's pouch facing the visceral surface of the right lobe of the liver (after Corning[7]).

The most prominent feature of the visceral surface is the renal fossa. Since this corresponds to the easily opacifiable posterior extension of the subhepatic space (Morison's pouch) (Fig. 2; and 4), the contours of this parenchymal indentation are clearly shown (Fig. 5; and 6). In addition, the anterior and posterior planes of the inferior visceral surface, ventral to the impression for the right kidney, are easily distinguishable (Fig. 5; and 6).

The margins of the anterior surface of the left lobe of the liver are clearly seen in prone Trendelenburg projections (Fig. 7). Difficulty is encountered in directing the contrast medium to reside on the visceral surface which is featureless and lies on a plane that is not struck tangentially by the roentgen-ray beam. However, the relationship of the undersurface of the left hepatic lobe to the anterior surface of the stomach and the lesser omentum may be occasionally demonstrated.

The positive contrast agent can be readily pooled around the gallbladder in prone or oblique projections to outline its position, size and configuration (Fig. 1, *A* and *B*; 6; 7; and 8). Demonstration of an enlarged gallbladder in a jaundiced patient indicates extrahepatic obstruction (Fig. 9).

The serosal surface of the stomach and its supporting mesenteries, the lesser omentum and the gastrocolic ligament, and thereby the thickness of the gastric wall are clearly outlined. Figure 10*A* illustrates the demonstration of gross extension of an unsuspected gastric malignancy in a cirrhotic male. Whereas the normal thickness of the greater curvature of the stomach is shown, peritoneography delineates a mass in the area of the gastrocolic ligament with disruption of the wall. This was not appreciated by peritoneoscopy. Only because of this finding on the peritoneogram, an upper gastrointestinal series was then done and showed the presence of an infiltrating gastric carcinoma (Fig. 10*B*). At surgery, extension through the wall into the gastrocolic ligament was confirmed. Large intraperitoneal masses may be present, but, because of their position, not indicated on routine barium contrast studies or visualized by peritoneoscopy. Figure 11, *A* and *B*, shows a 3.5 cm. metastatic mass on the lesser omentum. The detail of structures possible by peritoneography is



FIG. 5. Supine peritoneography. Positive contrast medium parallels the posteroinferior edge of the liver (arrowheads). Gas within Morison's pouch outlines the contours of the renal fossa on the posterior surface of the liver (arrows).

indicated by the demonstration of hypervascularity associated with the mass. Because of its lack of pressure on the lesser curvature of the stomach and its position deep to the liver, it was not seen on either upper gastrointestinal series or peritoneoscopy.

The double contrast examination also clearly visualizes the perisplenic compartment and its structures. The spleen is suspended in the left upper quadrant posteriorly by its ligamentous reflections (Fig. 12, *A* and *B*). All of these structures and the organs in intimate relationship with the spleen (Fig. 13) can be identified by peritoneography. The posterior border of the spleen extends medially behind the lienorenal ligament to be contiguous with the lateral margin of the left kidney and extends inferiorly, where it is in relationship to the splenic flexure of the colon and the phrenicocolic ligament[18] (Fig. 14; and 15). The anterior notched border of the spleen can be delicately outlined by con-

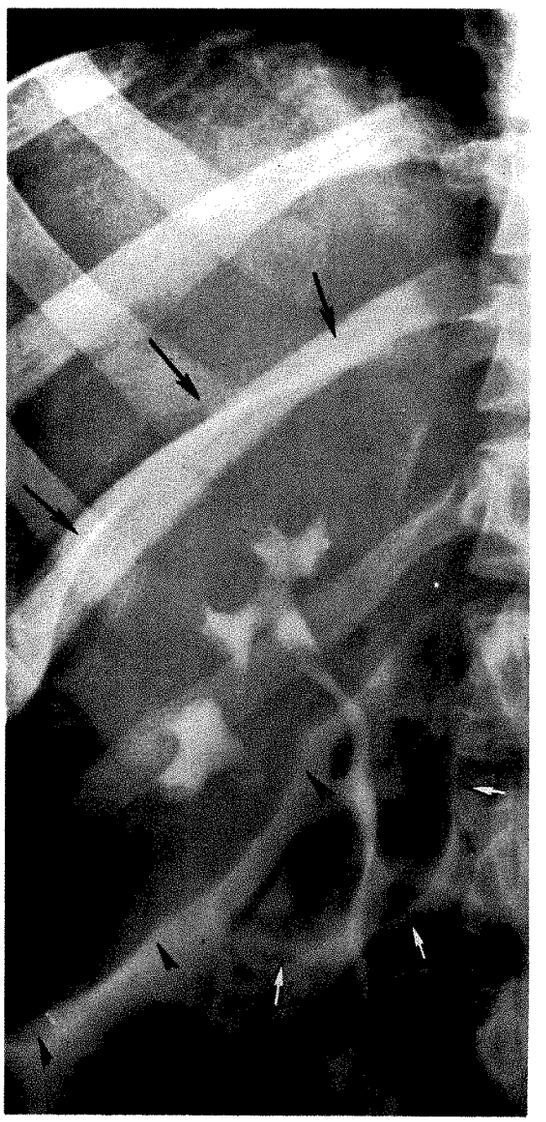


FIG. 6. Prone peritoneography. The inferior reflection of the coronary ligament, immediately below the bare area of the liver, is outlined (black arrows). Positive contrast medium along the notched anteroinferior border of the liver (arrowheads) pools around the "filling defect" of the gallbladder (white arrows).

trast medium on the gastrolienal ligament (Fig. 16). The tail of the pancreas is actually intraperitoneal in the sense that it is ensheathed between the leaves of the lienorenal ligament within the splenic hilus (Fig. 12, *A* and *B*). Since there is little peripancreatic fat in this area, it is not often demonstrated by retroperitoneal pneumography. Peritoneography, however, by the double contrast surrounding the posterior aspect of the lienorenal ligament, may outline the soft tissue density of the tail of the pancreas (Fig. 16).

The peritoneal recesses of the pelvis, including the 2 paravesical fossae and the midline rectovesical or rectouterine pouch (pouch of Douglas) are opacified in the horizontal supine position. In this way, peritoneography allows visualization of the thickness of the dome of the urinary bladder (Fig. 17) and the female reproductive organs (Fig. 18).

DISCUSSION

The study was well tolerated by all patients. They were not sensitive to the introduction of the contrast agent and suffered no untoward effects. While this small series does not lend itself to a statistical analysis, the clinical contribution in the cases studied became clear early in the course of the investigation. Peritoneography finally made or indicated the diagnosis in 4 cases, changed the clinical impression in 5, and confirmed the clinical diagnosis in 1.

Peritoneography is a simple, safe and reliable technique that can be done in any Department of Radiology. The diagnostic value of roentgenologically visualizing all intraperitoneal structures is apparent. The



Fig. 8. Prone peritoneography. A thin film of positive contrast medium clearly outlines the serosal contour of the gallbladder (gb).

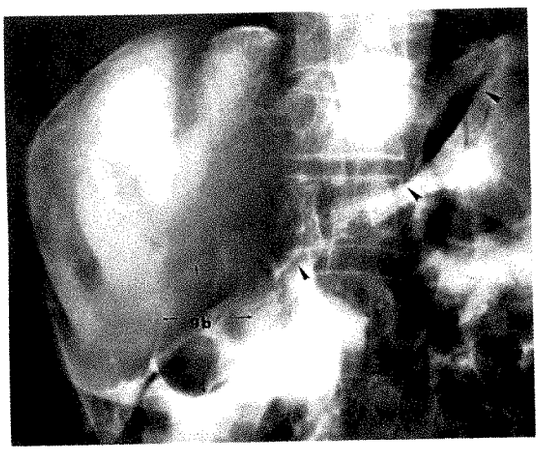


Fig. 7. Prone Trendelenburg position. The entire anterior contour of the liver, including the left lobe, is shown. Contrast medium pooling along the inferior liver edge (arrowheads) outlines the gallbladder (gb).

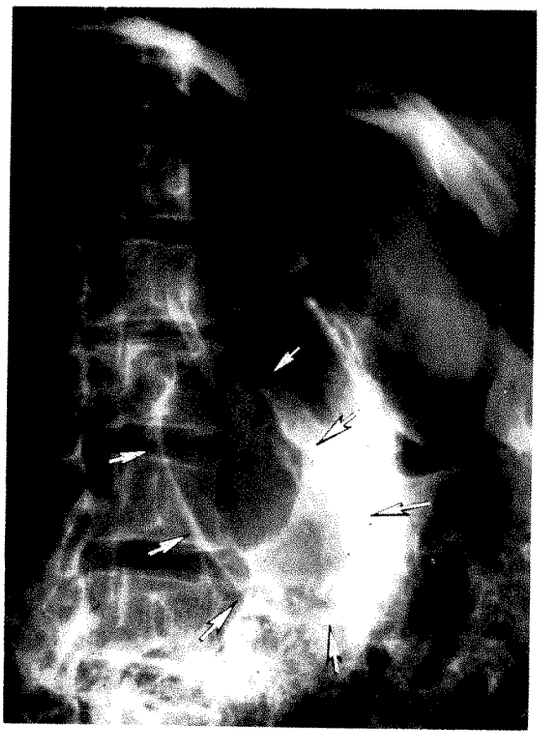


FIG. 9. Peritoneography. Right anterior oblique (RAO) Trendelenburg position. An enlarged gallbladder (arrows) in a jaundiced patient indicates extrahepatic obstruction.

clinical indications include: the evaluation of abdominal or pelvic masses noted roentgenologically or by physical examination; the extension of known or suspected malignant disease; the operability of patients with malignant tumors; the determination of the presence of a subacute or chronic subphrenic or subhepatic abscess; and to aid in the differentiation between intra- and extrahepatic jaundice.

Contraindications are easily established. Many are similar to those of routine intravenous urography. These include a history of allergy, multiple myeloma, or a blood urea nitrogen greater than 80 mg. per cent. Because of the elevation of the diaphragms produced by the gas, the study should not be undertaken in patients with pulmonary insufficiency. Because of the potential "third space" effect that the hyperosmotic contrast agent may induce, the study should be rigidly contraindicated in patients with borderline plasma volume. Moderate ascites is considered a relative contraindication, since excessive dilution of the opaque medium reduces detail.

Our routine filming now consists of a series of 10 projections: frontal and both oblique projections in the prone Trendelenburg (20°–30°) position; pos-

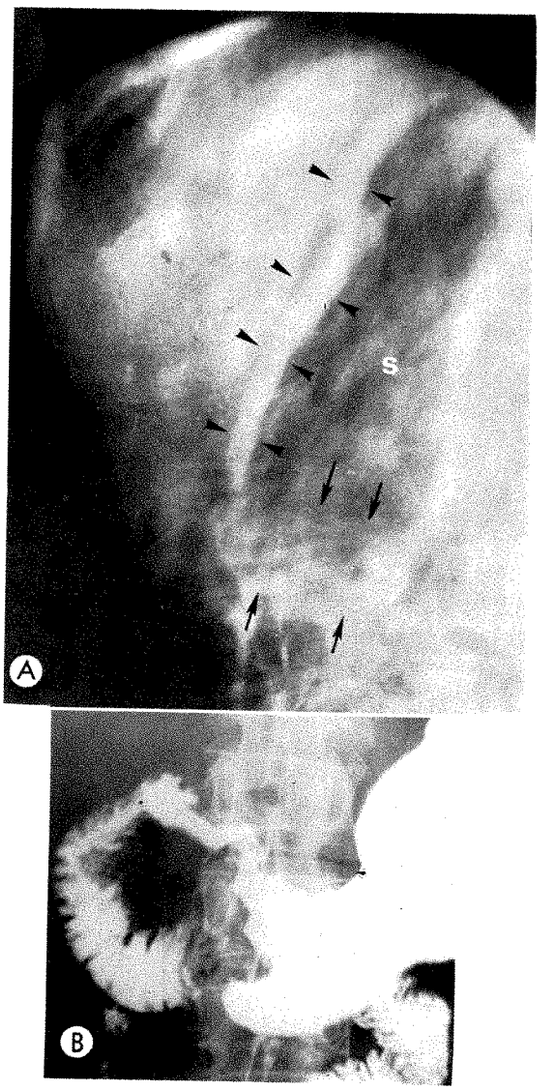
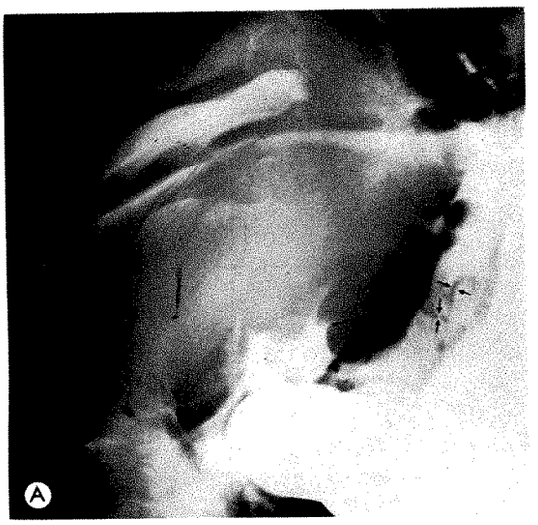


FIG. 10. (*A*) Peritoneography. Right lateral projection. The normal thickness of the greater curvature of the stomach (S) is shown (arrowheads), but it is disrupted along the distal pars media by an apparent mass (arrows) extending into the region of the gastrocolic ligament. Positive contrast medium has also extended into the right subphrenic space. (*B*) A subsequent gastrointestinal series demonstrates the intraluminal projections of an infiltrating carcinoma.



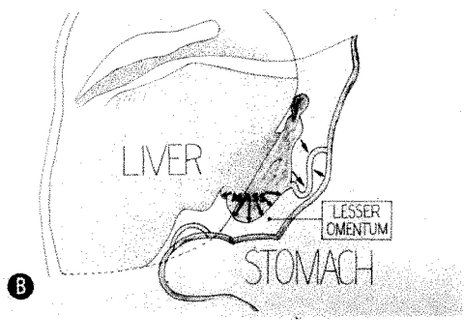


Fig. 11. (*A* and *B*) LAO prone peritoneography with simultaneous upper gastrointestinal series shows a 3.5 cm. metastatic mass (M) on the lesser omentum deep to the liver. Hypervascularity is indicated by the visualized serpentine "filling defect" of a tortuous vessel (small arrows). The normal thickness of the lesser curvature of the stomach is also shown.



Fig. 13. Supine peritoneography. Selective opacification outlines the margins of the spleen to the level inferiorly of the phrenicocolic ligament (arrow). (Reproduced with permission of *Radiology*.[18])

teroanterior, anteroposterior, and right and left lateral projections with the table horizontal; and then frontal and both oblique projections in the supine Trendelenburg (20°–30°) position. The contrast agent gravitates after introduction first to the pelvic recesses, so that in order to optimally visualize the upper abdominal structures, it is essential to begin with a prone Trendelenburg position. While decubitus and cross-table lateral views contribute to an understanding of the path-

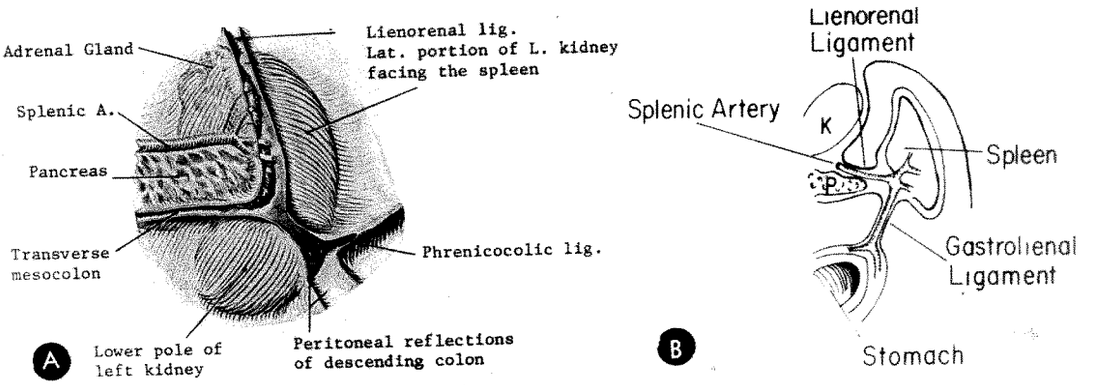


Fig. 12. (*A*) Posterior peritoneal attachments of the left upper quadrant (after Corning[7]). The spleen has been removed. (*B*) Diagrammatic transverse section with emphasis on the peritoneal attachments. The tail of the pancreas (P), anterior to the left kidney (K), resides within the lienorenal ligament. The perisplenic space is bounded by this and the gastrolienal ligament.

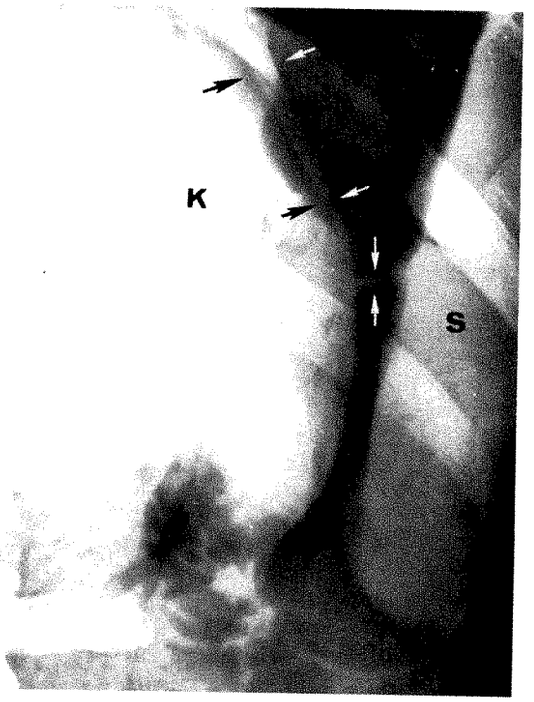


Fig. 14. Prone peritoneography, demonstrating the lienorenal ligament (arrows). S-Spleen; K-Kidney.

ways of flow of peritoneal fluid,[19] they give little additional anatomic information. Image-amplified fluoroscopy is helpful, but not indispensable. With experience, fluoroscopy with controlled positioning of the patient, to selectively opacify a particular area, may be either delayed until after the roentgenography or found unnecessary altogether. The presence of intraperitoneal gas enhances the positive contrast and compensates to some degree for the effect of gravity in positioning. About 80 per cent of the nitrous oxide is absorbed within 2 hours.[25] No erect roentgenograms are obtained since hypotension, especially in the elderly, is common in pneumoperitoneography in the upright position. Only 15 to 20 minutes are required for the introduction of the double contrast medium and the completion of the radiography. It is our intention to employ more commonly simultaneous conventional intraluminal contrast studies. We expect this to provide more detailed parameters of wall thickness and transmural extension of disease.

Water-soluble opaque media possess several desirable qualities in addition to their safety. They diffuse throughout the peritoneal cavity and yet can be controlled by gravity, pressure and site of instillation. Roentgenographic contrast is controllable over a wide range. The agent is readily absorbed from the peritoneal surfaces. Opacification of the kidneys and urinary bladder occurs within 20 to 30 minutes and there is no trace of positive contrast material in the peritoneal cavity on 3 hour roentgenograms. This clinically confirms experimental observations.[14] The coincident urogram obtained is very useful to complement the opacification of the peritoneal cavity itself. Some diuresis, as in intravenous drip urography, follows the procedure.

Renografin 60 has a virtually neutral pH, but is approximately 6 times hypertonic.

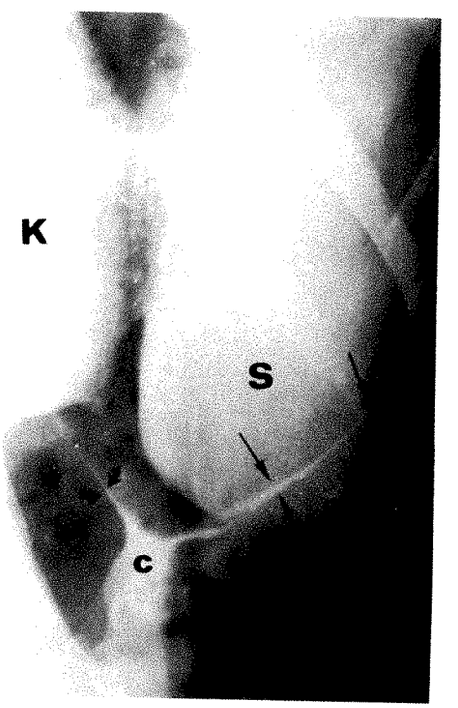


Fig. 15. Prone peritoneography outlines the phrenicocolic ligament (long arrows) supporting the spleen (S) as it extends from the splenic flexure of the colon (c) to the left diaphragm, and its continuity with the gastrolienal ligament (small arrows) seen on end. The close relationship of the posterior margin of the spleen to the left kidney (K) is shown.

With the dilution used and its rapid rate of absorption, there is no clinically appreciable ascites. Some ascitic fluid is undoubtedly transiently induced, however, since the contrast medium is progressively diluted. Roentgenograms should, therefore, not be greatly delayed. Large quantities of fluid can be absorbed from the peritoneal cavity.[13] In animals, the ascites induced by the intraperitoneal injection of large amounts of hypertonic water-soluble contrast agents is completely resorbed between 2 and 24 hours.[15,16]

Peritoneoscopy, with a rigid tube and a small lens system, allows direct visualization of a limited portion of the abdominal contents. Its greatest and most consistent contribution is in the diagnosis of cirrhosis and widespread peritoneal disease.[30] A relatively small area of the anterosuperior aspect of the liver and the upper small bowel loops and parietal peritoneum are the usual structures seen. Great limitations are imposed by obesity and the presence of adhesions. Indeed, a previous abdominal operation is generally a contraindication to peritoneoscopy for fear of transecting a vascular adhesion with insertion and movement of the instrument. Results of this study show that the double-contrast examination is a valuable complement, if not alternative, to peritoneoscopy.

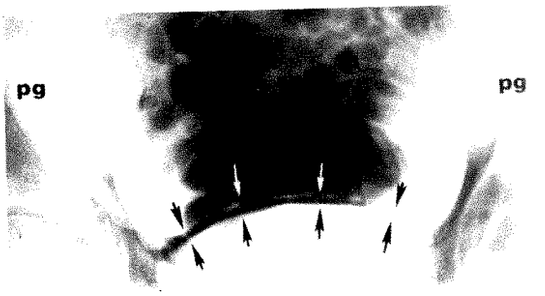


FIG. 17. Supine peritoneography. Contrast medium gravitates to the pelvic cavity. With renal excretion and opacification of the urine, the thickness of the dome of the urinary bladder can be ascertained (arrows). Fluid begins to ascend both paracolic gutters (pg). The external contours of the sigmoid colon and small intestinal loops are outlined.



FIG. 16. Prone peritoneography. The tail of the pancreas, ensheathed within the leaves of the lienorenal ligament, is outlined (arrows). It is directed toward the splenic hilus, between the anterior notched border of the spleen (arrowheads) indicated by contrast medium apposing the gastrolienal ligament (GL) and the more medial posterior margin in relationship to the left kidney. Compare to Figure 12*A*.

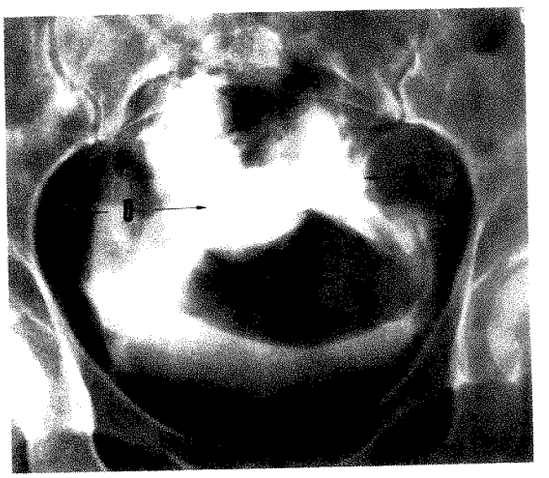


FIG. 18. Supine peritoneography. The uterus (U) and both ovaries (O) are shown. Enlargement of the right ovary was proved to be secondary to endometriosis.

Peritoneography has been shown in this series to be capable of identifying both the presence and extent of intraabdominal disease, which may not be recognized by either routine contrast studies of the alimentary tract or direct visualization *via* peritoneoscopy.

SUMMARY

A technique providing precise delineation of the peritoneal cavity and its contents is described.

Peritoneography, the intraperitoneal instillation of a water-soluble contrast medium and gas, is a safe and practical method of clinical examination which extends the roentgenologic diagnostic capabilities in intraabdominal disease.

It enables the roentgenographic visualization and determination of external surfaces and contours of abdominal viscera, peritoneal reflections and recesses, and the thickness of the wall of portions of the alimentary tract. It may demonstrate more structures and lesions than can be accomplished through direct visualization by peritoneoscopy.

Peritoneography is clearly capable of identifying both the presence and extent of intraabdominal disease which may not be recognized by either routine contrast studies of the alimentary tract or peritoneoscopy.

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COMBINED OCCURRENCE OF RETROPNEUMOPERITONEUM AND PNEUMOPERITONEUM*

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ALTHOUGH both pneumoperitoneum and retropneumoperitoneum are quite common, the combined occurrence of free air in the retroperitoneal and peritoneal spaces is extremely rare. Isolated cases have been reported following rectal biopsy,[2] abdominal laparotomy,[1] rupture of the third portion of the duodenum,[6] or complicating diagnostic retropneumoperitoneum.[4]

Two recent cases of simultaneous retropneumoperitoneum and pneumoperitoneum have prompted a review of the anatomy, direction of spread, and roentgen manifestations of this unusual clinical entity.

REPORT OF CASES

CASE I. A 50 year old woman underwent an office proctoscopic examination as part of a yearly physical examination. The rectosigmoid was normal to 25 cm. with the exception of a single 1 cm. sessile polyp located on the left posterior rectosigmoid wall at 15 cm. The lesion appeared benign and was removed with biopsy forceps. The patient tolerated the procedure well and was asymptomatic at its completion.

Following the sigmoidoscopy the patient was sent to the hospital radiology department for a previously scheduled oral cholecystography. The roentgenograms revealed the presence of retroperitoneal air outlining the right kidney and adrenal (Fig. 1*A*). In addition, a horizontal accumulation of air outlining the center of the diaphragm was noted.

The patient's physician was alerted and the patient was admitted to the hospital. On admission, 2 hours after the sigmoidoscopy, she complained of dull ache in the abdomen and bilateral shoulder pain.

Physical examination revealed an alert patient in no distress with a blood pressure of 120/80 mm. Hg and a pulse rate of 92. The oral temperature was 100.2° F. The abdomen was soft but diffusely tender. The tenderness was greater in the left lower quadrant where mild guarding and rebound tenderness were elicited. The bowel sounds were normal.

Roentgenograms of the abdomen, including an upright roentgenogram of the chest, revealed a combination of retropneumoperitoneum and pneumoperitoneum. The supine roentgenogram of the abdomen (Fig. 1*B*) showed air outlining both kidneys and adrenals. The upright and decubitus roentgenograms of the abdomen and chest (Fig. 1*C*) demonstrated free air under the diaphragm and pneumomediastinum. The center of the diaphragm was outlined by air which had dissected between the peritoneum and fascia of the diaphragm.

The patient underwent exploratory laparotomy through a midline incision. A small amount of cloudy fluid was found in the pelvis. A subserosal hematoma was seen on the left side of the sigmoid colon and a small perforation was noted in the serosa on the anterior surface of the sigmoid. The serosa was incised at this point and dissection was carried posteriorly. A 0.5 cm. opening in the bowel wall was found on the left posterior surface of the sigmoid, approximately 3 cm. from the serosal opening located on the anterior wall. Air apparently had dissected posteriorly through the sigmoid mesentery into the retroperitoneal space and anteriorly beneath the serosa of the sigmoid to its antimesenteric surface where it perforated the serosa entering the peritoneal space. The initial posterior perforation had occurred through the base of a small diverticulum.

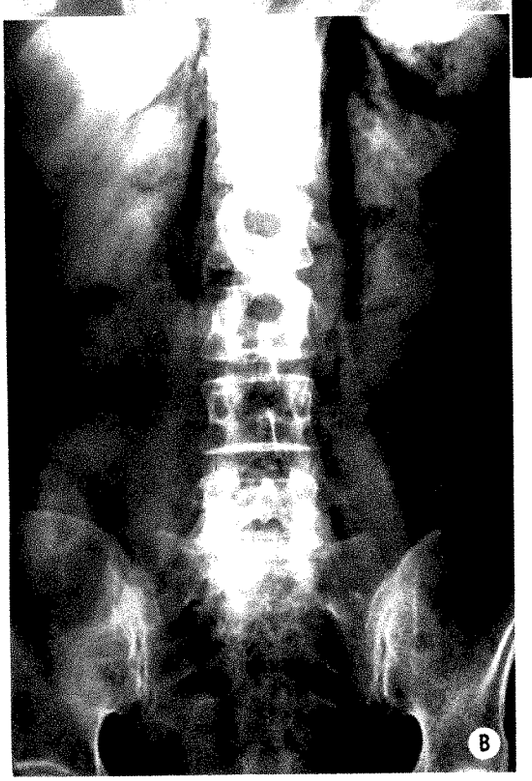
The colon was repaired in 2 layers, the pelvis was drained and the abdomen was closed.

The patient made an uneventful recovery and was discharged on the fourteenth postoperative day.

CASE II. A 37 year old woman with known renal tubular acidosis and multiple renal calculi, was admitted to the hospital because of severe right flank pain. The intravenous pyelogram showed a hydronephrotic right col-

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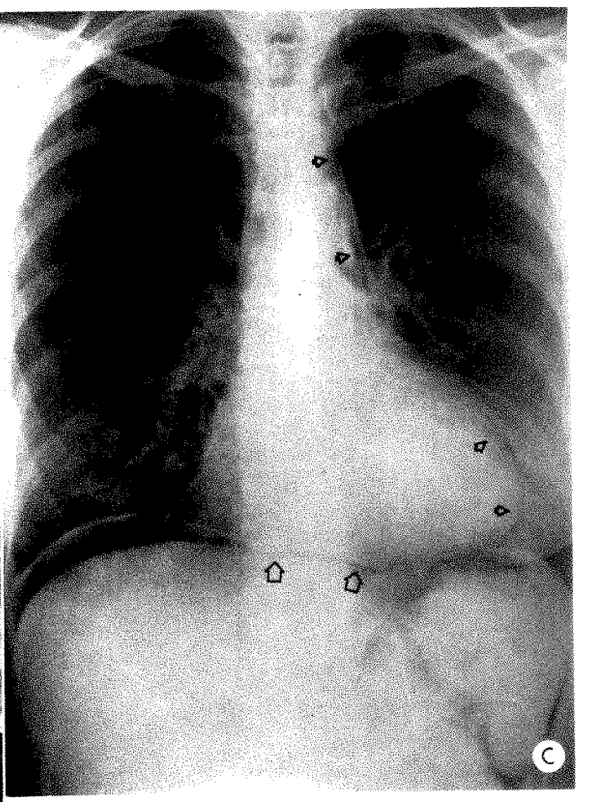


FIG. 1. Case 1. (*A*) Prone oblique roentgenogram from oral cholecystography, taken approximately half an hour after a sigmoid polyp biopsy. The air in the retroperitoneal space outlines the right kidney and adrenal. Note the crus of the diaphragm. (*B*) Supine roentgenogram of the abdomen and (*C*) upright roentgenogram of the chest taken 2 hours after *A*. Both kidneys and adrenals are outlined by streaky accumulations of air. The pneumoperitoneum is seen on the chest roentgenogram. Note the pneumomediastinum and the pericardium (small arrows). The air outlining the aponeurotic portion of the diaphragm (large arrows) does not change position in *A* and *C*. It represents air dissecting between the peritoneum and the fascia covering the diaphragm.

lecting system and a nonfunctioning left kidney. Multiple calculi in the right kidney and a single calculus in the left ureter, near the bladder were also noted. A renogram showed an obstructive pattern on the right and no function on the left. Two unsuccessful attempts were made to remove the left ureteral calculus during cystoscopy. After the second manipulation, catheters were left in both ureters and 6,000 cc. of urine was collected in 12 hours.

A few days later the patient was taken to the operating room, where both flanks were explored. Under general anesthesia the retroperitoneal space was entered on each side through separate incisions extending from the tip of the eleventh rib down to the lateral border of the rectus sheath. One large and 2 small calculi were removed from the right ureter with the Dormia basket extractor manipulated through a ureteral incision. On the left side, a single calculus was removed by an incision of the ureter directly over the calculus. Both ureterostomies were closed with No. 5-0 chromic sutures. HemoVac drains were then placed down to the ureters on both sides. The surgical incisions were closed and the patient was taken to the recovery room, where suction was applied to the HemoVac drains.

The patient had a temperature elevation to 102.0° F. on the first postoperative day and there were rales at both lung bases. The ureteral catheters were removed but the HemoVac suction continued. On the second postoperative day the patient developed tachycardia, respiratory distress, and marked abdominal distention. The abdomen was tympanitic on percussion.

Roentgenograms of the abdomen and an upright view of the chest were obtained which showed large amounts of retroperitoneal and intraperitoneal air (Fig. 2, *A–C*). The retropneumoperitoneum was manifested by a streaky accumulation of air about the kidneys and ureters. The urinary bladder was outlined and air was seen in both inguinal regions. On the upright roentgenograms, intraperitoneal air was seen outlining the liver and spleen. On the decubitus roentgenograms, free air was noted between loops of small bowel.

Re-examination of the patient revealed that the air shield suction apparatus had been improperly connected to the HemoVac drainage tubes so that for several hours, instead of suction, air was being pumped into the patient's retroperitoneal space.

Eighteen gauge needles were inserted on each side of the abdomen close to the flanks. Large amounts of air escaped through the needles and the abdomen was rapidly decompressed.

The temperature returned to normal in the next few days and on the eleventh postoperative day the patient was discharged.

DISCUSSION

Retropneumoperitoneal air may result from diagnostic pneumography,[11,13] peptic, traumatic[6,7] or iatrogenic[2,3] perforation of a hollow viscus, infection with a gas forming organism or as complication of pneumatosis intestinalis.[8] The air is usually confined to the retroperitoneal space, but it may find its way into the subcutaneous tissue,[2] the mediastinum[9] or rarely the peritoneal space.[4] Pneumoperitoneum on the other hand, is most commonly seen after abdominal surgery, but may also be caused by a perforated hollow viscus, tubal insufflation, or intraperitoneal infection with gas forming organisms.

Both of the reported cases illustrate iatrogenic introduction of air into the retroperitoneal space with subsequent dissection into the peritoneal space.

In the first case, perforation of the lower sigmoid caused a subserosal accumulation of air which rapidly dissected posteriorly between the leaves of the sigmoid mesentery to enter and diffuse through the retroperitoneal space. As air and blood continued to accumulate within the mesentery, the serosa was slowly dissected from the bowel wall eventually perforating at its thinnest point on the antimesenteric surface of the sigmoid colon. Air then entered the free peritoneal space and later roentgenograms revealed a combined pneumoperitoneum and retropneumoperitoneum.

In the second case, a tremendous amount of air was inadvertently pumped into the retroperitoneal space. The air dissected in the loose areolar tissue between fascial planes and as the pressure increased, it eventually burst through a point in the posterior parietal peritoneum to enter the peritoneal space.

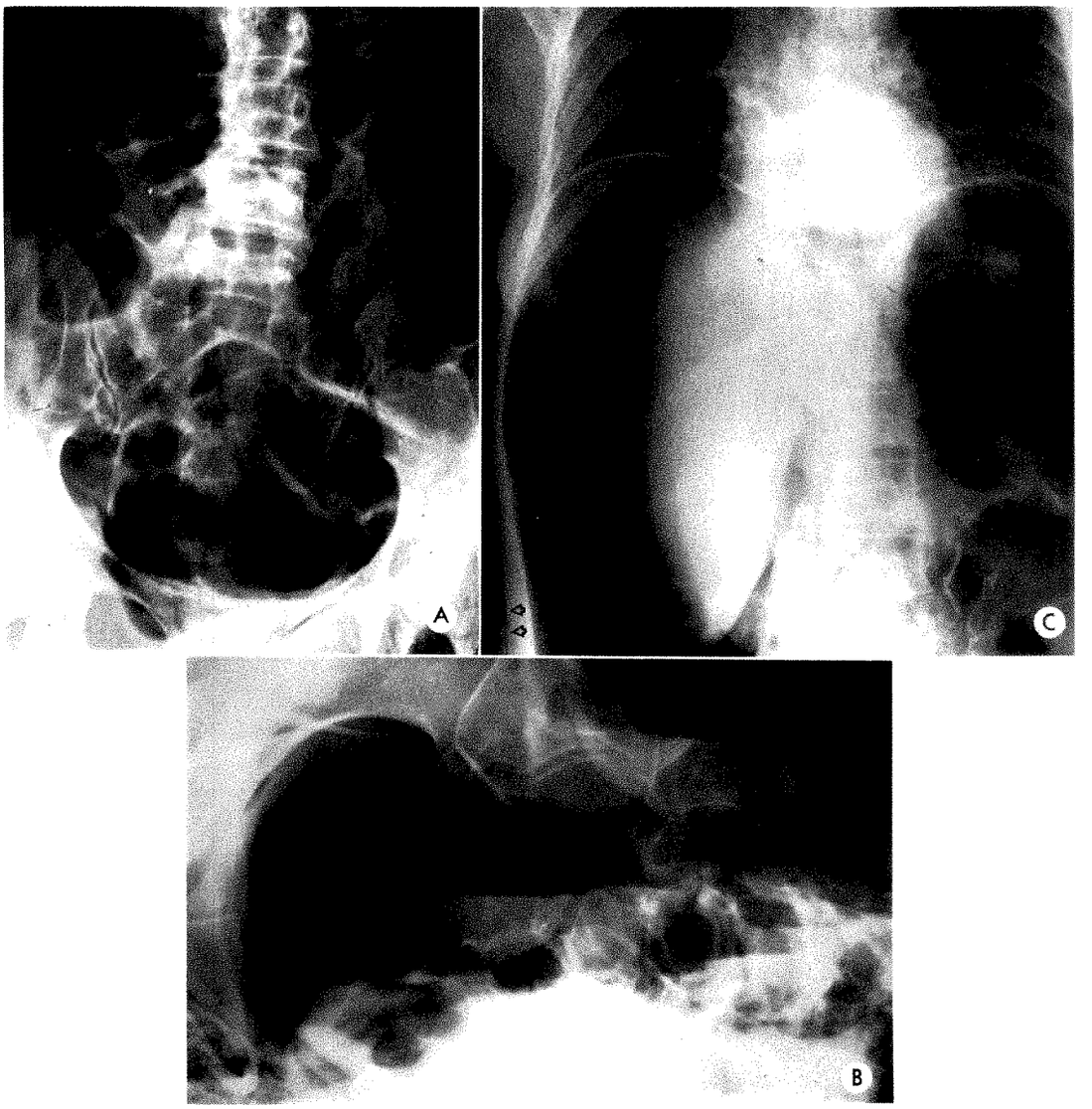


Fig. 2. Case II. (*A*) Supine roentgenogram taken after inadvertent reversal of retroperitoneal suction. The streaky air collections about the left ureter represent the retropneumoperitoneum. The urinary bladder is outlined by retroperitoneal air. There is air in the left inguinal area. The large air accumulation in the flanks and the outlined bowel wall represent pneumoperitoneum. (*B*) The intraperitoneal air on this decubitus roentgenogram outlines the uterus and right ovary. Note emphysema in the left groin. (*C*) The large pneumoperitoneum has displaced the liver and spleen medially and downwards (upright roentgenogram). Note the small extraperitoneal collection of air (arrows).

ANATOMY

The manner in which free air enters both the intraperitoneal and retroperitoneal spaces is easily explained once the anatomy is understood. The peritoneal "cavity" is actually a potential space which is easily distended by air or fluid. Except in females where access to the vagina potentially exists, the peritoneal space is a closed sac bounded by parietal and visceral peritoneum and limited superiorly by the diaphragm and inferiorly by the pelvic diaphragm. Although it communicates readily with the lesser sac through the

foramen of Winslow, there is no communication to the retroperitoneal space.

The retroperitoneal space is filled with loose areolar tissue, connective tissue and many abdominal organs. The kidneys, ureters, adrenals, pancreas, second, third, and most of the fourth portion of the duodenum, most of the mesentery, transverse and sigmoid mesocolon, aorta, inferior vena cava, broad ligaments, and the bare area of the liver, all lie within the retroperitoneal space. The retroperitoneal space is not a closed sac, but communicates superiorly with the posterior mediastinum through the aortic hiatus of the diaphragm and inferiorly with both groins through the femoral canal.

Contrary to the peritoneal space, the retroperitoneal space is not easily distended. A small amount of air will be trapped locally between strands of loose areolar tissue. On the other hand, large amounts of air will be forced out of the local area following both vertical and horizontal pathways.

DIRECTIONS OF SPREAD

Retroperitoneal air spreading horizontally finds its way into the subcutaneous tissues of the flanks and anterior abdominal wall where it is recognized clinically as subcutaneous emphysema. However, most of the air spreads vertically.

Rivas[13] has shown that air injected near the sacrococcygeal joint is detected roentgenographically in the mediastinum, neck, retroperitoneum, pelvis, and limbs. Mitchell[12] experimentally demonstrated the route of vertical spread by injecting barium in the perinephric region of stillborn infants. After filling the renal fossa, the barium spreads downwards to the pelvis and into the inguinal area. In the lower lumbar region, the barium crossed to the contralateral side of the abdomen and then spread upwards along the inferior vena cava. Others have demonstrated that air follows the great vessels superiorly into the mediastinum and neck and inferiorly into the inguinal area and lower extremities.[4] Similarly, air may pass downwards into the retroperitoneal space from above. In 1939, Macklin[10] showed experimentally that overinflation of pulmonary alveoli led to rupture and air leak into the pulmonary interstitial spaces. From there the air followed the sheaths of the pulmonary vessels to the root of the lung, thence to the mediastinum, retroperitoneal space, groin, and leg. Clinical examples of this route of spread have also been reported.[5]

Although the retroperitoneal space does not communicate with the peritoneal space, air may find its way into the peritoneal space by one of two mechanisms. Retroperitoneal air following blood vessels may dissect into the mesocolon separating the serosa from the bowel wall with eventual perforation. This means of spread has been experimentally produced by Keyting *et al.*[8] and appears to be the route of spread taken in the first case described here. Alternatively, massive retroperitoneal collections of air may perforate the posterior parietal peritoneum entering the peritoneal space without involving the bowel wall. This route of spread was demonstrated by our second case.

These anatomic relationships and experimental data suggest that the combined occurrence of pneumoperitoneum usually originates within the retroperitoneal space. Intraperitoneal air leaks readily expand the distensible peritoneal space. Only when extensive dissection of the retroperitoneal tissues occurs during abdominal laparotomy would one expect to find retroperitoneal air originating from the peritoneal space. On the other hand, air within the poorly distensible retroperitoneal space seeks egress. Extending vertically and horizontally, it may also enter the peritoneal space by the 2 routes described.

ROENTGEN MANIFESTATIONS

The roentgen signs of pneumoperitoneum are well known. On the supine roentgenograms, the dome sign, the falciform ligament sign, and the bowel wall outline can be seen. On the upright and decubitus roentgenograms, free air can be demon-

strated. However, these findings may be obscured with the combined occurrence with retropneumoperitoneum.

If free air is found in the abdomen other than under the diaphragm, a retroperitoneal air accumulation must be suspected.[1] The retroperitoneum, while one continuous space, is loosely divided by areolar tissue septa. This results in a streaky appearance of the air and explains its fixation with changes in the patient's position.

Gould and Thorwarth[6] have described roentgen signs of retroperitoneal rupture of the duodenum. These signs are valid for any accumulation of retroperitoneal air and include: bubbles, sheets or pockets of air outlining one or both kidneys, air along the psoas muscles, retroperitoneal air in the infradiaphragmatic and pelvic regions, mediastinal and cervical emphysema, subcutaneous emphysema of the flanks and finally encapsulated or free intraperitoneal air.

It is important to recognize the presence of air in the lesser sac and retroperitoneal air outlining the aponeurotic portion of the diaphragm (Fig. 1, *A* and *C*). Air in the lesser sac is seen on the upright roentgenogram in the right paravertebral region having a curvilinear border and on the supine roentgenogram as an air collection high up under the diaphragm.[1]

When evaluating roentgenograms on which there is a combined occurrence of retropneumoperitoneum and pneumoperitoneum, one may be tempted to locate the source of the air leak by determining which space has the largest accumulation of air. This is hazardous because the limited distensibility of the retroperitoneum will usually result in a larger pneumoperitoneum regardless of the location of the leak. Unless the patient has undergone abdominal surgery with dissection of the posterior parietal peritoneum, the air will almost invariably have arisen within the retroperitoneal space.

An attempt should be made to establish the direction of spread of the retroperitoneal air and this usually requires repeated roentgen examinations. If air is recognized in the lesser sac and in the extraperitoneal soft tissue of the abdominal wall before it is seen in the mediastinum, the retropneumoperitoneum probably spread in the horizontal fashion from an origin in the retroperitoneal space. If air is found in the mediastinum and neck before it is seen retroperitoneally, its origin must be above the diaphragm. The study of the roentgenograms for directions of spread may help to localize the source of the air leak, thus aiding the clinician in management of the patient.

SUMMARY

A combined occurrence of massive retropneumoperitoneum and pneumoperitoneum is rare.

Two recent cases are reported: one resulting from an iatrogenic perforation of the sigmoid; and the other from an inadvertent introduction of air into the retroperitoneal space.

The anatomic relationships, directions of spread, and the roentgen manifestations of a combined occurrence of retropneumoperitoneum and pneumoperitoneum are discussed.

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SCANNING OF THE HEPATIC BLOOD POOL IN LIVER AMEBIASIS*

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LIVER scanning with radiocolloids has become an important method for the diagnosis and localization of intrahepatic lesions such as primary[3,32] or metastatic[26] tumors, cysts[25] and pyogenic[24] or amebic[5,6] abscesses. It has proven to be more accurate than the usual roentgenologic procedures,[15] liver function tests[12,15] and liver biopsies,[12] and to have a similar diagnostic precision to that of splenoportography[28] and celiac axis angiography.[17,30] However, when the abscess is lodged near the surface of the liver, it can be difficult to ascertain its actual size and boundaries due to the congestive processes encircling the lesion itself,[2] interfering with the normal phagocytic activity of the reticuloendothelial tissue and decreasing the concentration of radiocolloids in this area. On the other hand, it has been shown elsewhere, that this same area is affected by an increased vascularization.[30]

This study was designed to explore a possible improvement on the imaging of liver abscesses by the use of transferrin-bound In^{113m} as a label for the hepatic blood pool.

MATERIAL AND METHOD

One hundred and twenty-five patients with amebic abscesses of the liver were included in this study. The diagnosis was confirmed by the response to medical treatment, diagnostic puncture or laparotomy. In fatal cases the scintigraphic findings were confirmed by necrospy.

Liver scans with iron and In^{113m} coprecipitates (2–2.5 mc) were first obtained in each patient. A second scan was obtained a few hours later by using transferrin-bound In^{113m} (2–2.5 mc) to depict the distribution of hepatic blood pool. Anterior, posterior and right lateral projections of the liver were obtained in either case by using a 5 inch rectilinear scanner. For a better comparison of the resulting images, these were digitalized according to 4 different levels of radioactivity: 0 to 25 per cent; 26 to 50 per cent; 51 to 75 per cent; and 76 to 100 per cent of maximum count rate. The areas of the concentration defects observed in the first scan were compared with those observed in the second scan.

RADIOPHARMACEUTICALS

Indium 113m was eluted with 0.5 *N* HCl from a modified, sterile Sn^{113}-In^{113m} generator system (Union Carbide).[4]

In^{113m} colloid was prepared in our laboratory using the method of Adatepe *et al.*:[1] Fe^{+++} (50 μg. in 0.05 ml.) was added to carrier-free, ionic In^{113m}, followed by 1.5 ml. of phosphate buffer (pH 7.4) and injected intravenously.

For the study of hepatic blood pool, sterile, carrier-free, ionic In^{113m}, as eluted from the generator (pH 1.4 to 1.7) was administered intravenously.[22]

RESULTS

Arterial and venous phases of celiac axis angiography, in a case of acute amebic abscess of the liver, are shown in Figure 1, *A* and *B*. Both images demonstrated a conspicuous increase of vascularity in the hepatic tissue surrounding the lesion.

All the liver scans obtained with colloidal In^{113m} showed one or more concentration defects. Ninety-eight of them (78.4 per cent) had single defects, while 27 (21.6 per cent) depicted multiple defects. On the other hand, scanning of the hepatic blood pool with transferrin-bound In^{113m} demonstrated single defects in 89 cases (71.2

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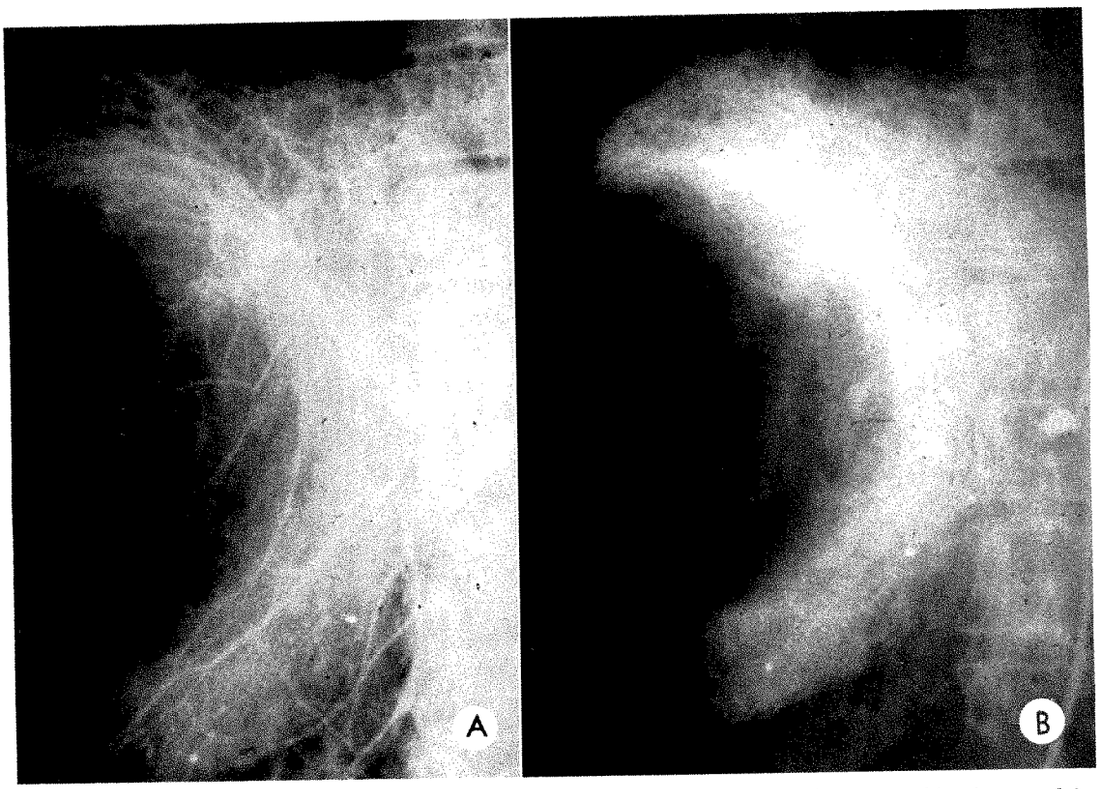


FIG. 1. (*A*) Arterial and (*B*) venous phases of celiac axis angiography in a case of acute amebic abscess of the liver, showing increased vascularity in the tissue surrounding the lesion.

per cent) and multiple defects in 36 (28.8 per cent).

All the liver scans obtained with In^{113m}-transferrin showed a remarkable decrease in the size of the filling defects when compared with the corresponding images obtained with colloidal In^{113m}. On an average, the size of the defects observed in the images obtained with ionic In^{113m} was 23.9 per cent $\pm$ 8.2 of the size of the lesions depicted by scintigraphy with the radiocolloid.

Figure 2*A* shows a liver scan obtained with colloidal In^{113m} in a patient with typical symptoms of an amebic hepatic abscess. It showed a normal sized liver image, with homogeneous distribution of the radiocolloid and some indentations at the lower profile of the left lobe. A few hours later, another scan was obtained after intravenous injection of carrier-free, ionic In^{113m} (Fig. 2*B*). It showed the distribution of the blood pool of the liver, heart and aorta, demonstrating a conspicuous increase in size of the hepatic left lobe and 2 well outlined areas without radioactivity in this lobe, corresponding perfectly to the indentations found in the previous study.

Figure 3*A* shows a liver image obtained with colloidal In^{113m} that resembles a normal variant described by McAfee *et al.*[20] as liver "en chapeau du gendarme," which they found in 14 per cent of normal cases. Nevertheless, scintigraphy with carrier-free, ionic In^{113m} demonstrated a clear-cut defect at the upper region of the hepatic left lobe, which was limited by the blood pools of the liver and heart (Fig. 3*B*).

When the abscesses are located near the surface of the liver, scanning of this organ with radiocolloids is not enough to obtain actual information about its size and shape

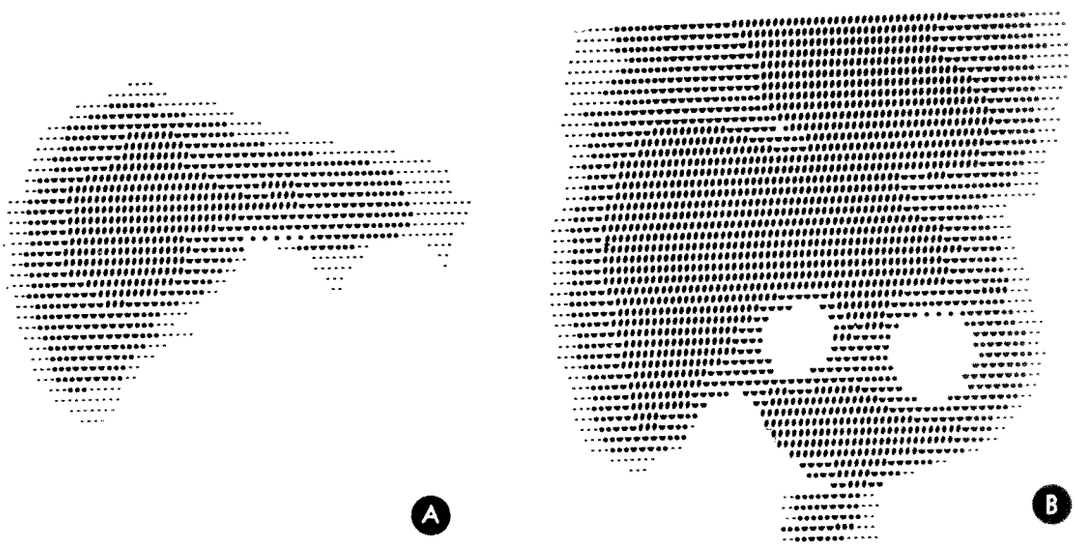


FIG. 2. Two amebic lesions in the left hepatic lobe. (*A*) Scan obtained with colloidal In^{113m}; and (*B*) scan obtained with ionic In^{113m}, clearly demonstrate the hepatic blood pool around the lesions.

and about its relationship with the hepatic surface or with another abscess due to the process that interferes with phagocytosis in the surrounding tissue. This is of paramount importance when the abscess is lodged near the lower surface of the liver as it may imply the risk of a spontaneous rupture into the abdominal cavity (Fig. 4*A*). In such cases, scanning with ionic, carrier-free In^{113m} proved to be useful, since

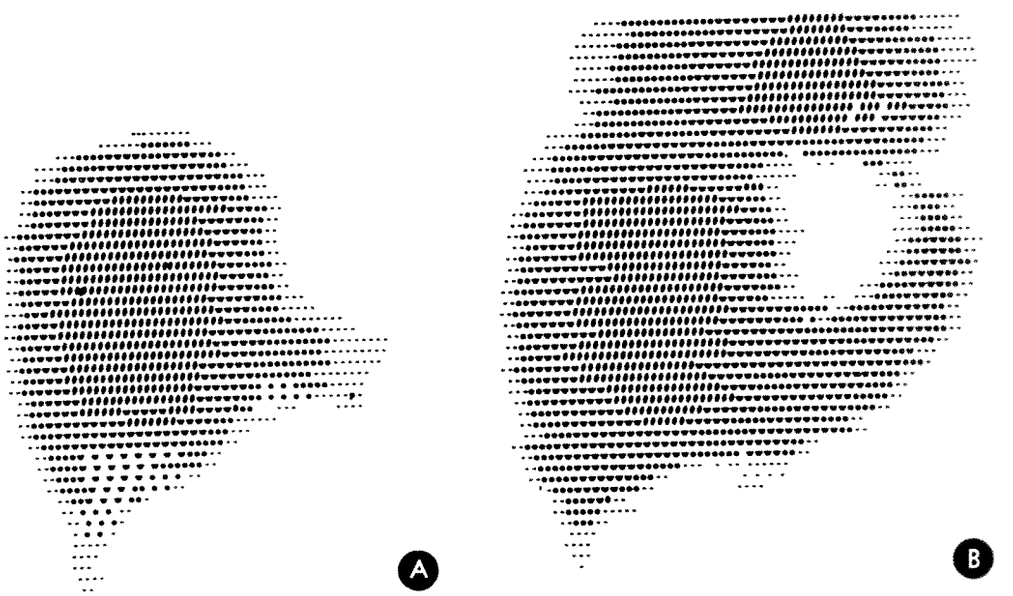


FIG. 3. An amebic abscess located in the upper region of the left hepatic lobe. (*A*) Scan obtained with colloidal In^{113m}; and (*B*) scan obtained with ionic In^{113m}, show the lesion delimited by cardiac and hepatic blood pools.

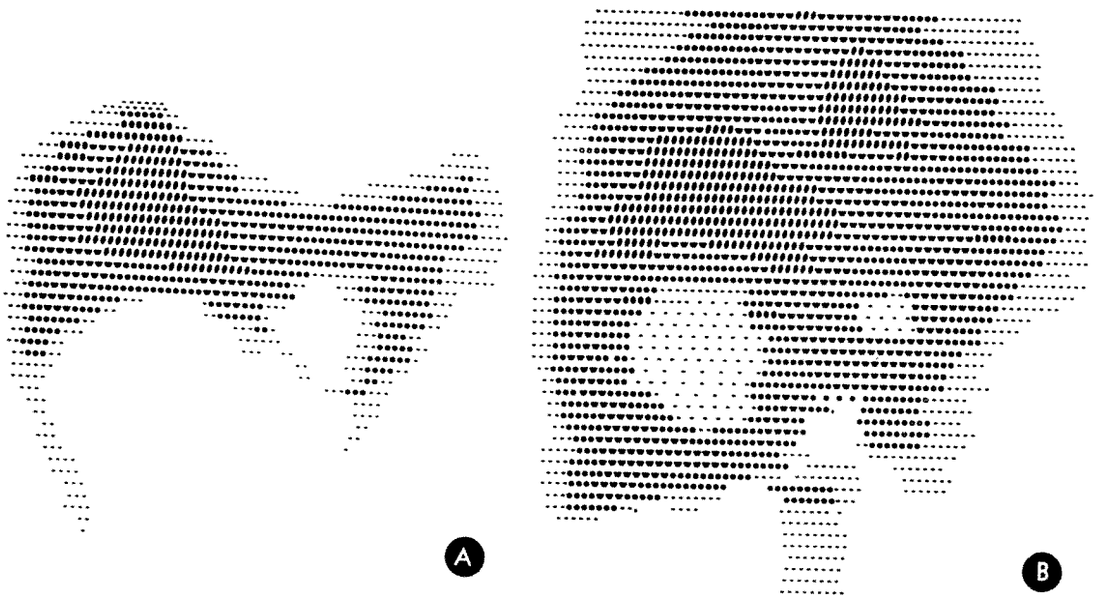


FIG. 4. Large abscess in the lower region of the right hepatic lobe and a small lesion in the left lobe. (*A*) Scan obtained with colloidal In^{113m}; and (*B*) scan obtained with ionic In^{113m}, show the hepatic blood pool encircling the lesions.

it labels the blood pool encircling the abscess and thus the actual boundaries of the lesion can be well defined (Fig. 4*B*).

DISCUSSION

A hepatic abscess is the natural consequence of the invasion of the liver by trophozoites of *Entamoeba histolytica*, carried from the intestine through the portal vein and distributed in the liver parenchyma according to its intrahepatic branches,[7] producing tissue destruction probably by some cytolytic process. These necrotic areas are variable in size and number, containing tissue debris and are surrounded by a zone of hyperemic tissue.[2,31]

Absence of functioning reticuloendothelial tissue in these lesions is the reason for liver scanning with radiocolloids in the study of hepatic abscesses. These appear in the scan image as empty spaces surrounded by the radioactivity present in the normally functioning hepatic reticuloendothelial system. However, in some instances, it is difficult to ascertain the actual size and boundaries of the lesion due to the process encircling the abscess, which interferes with the normal phagocytic activity of the reticuloendothelial system in this region.

The process at the periphery of the abscess is depicted by angiography as a hyperemic area surrounding the abscess itself (Fig. 1, *A* and *B*). This fact suggested the use of a plasma label in order to obtain scintigraphic images of the distribution of the hepatic vascular bed to gather more precise information about the actual size and limits of the abscess.

In 1967, Stern *et al.*[29] demonstrated that the distribution of carrier-free, ionic In^{113m} in the organism depends principally on the pH of its solution. At pH lower than 4.0, this radionuclide is bound, as a cation, to a beta globulin known as transferrin. In this condition, its half time in blood is between 2.0 to 3.5 hours, without significant excretion by the urine.

Soon, this new radiopharmaceutical was used as a label for scanning the placental blood pool[18,21,22,27,29,34] and for imaging of the cardiac blood pool for diagnosis of pericardial effusion.[27,29] It has also been used for estimating the plasma volume[33] and the cardiac output.[16]

In 1969, the method for producing this

radiopharmaceutical was greatly simplified by our group,[8,22] when it was observed that heating at 50°C. and the addition of gelatin to carrier-free In^{113m} was unnecessary and that this radionuclide, when injected as eluted from the generator system, at pH 1.4 to 1.7, is strongly bound *in vivo* by serum transferrin.

In the same year a series of encouraging reports appeared on the use of this radiopharmaceutical in the study of liver abscesses, to differentiate this type of lesion from other space-occupying masses of the liver.[8–11,13,14,23] In 1970, Lubin and associates[19] reported their results with this compound in the differential diagnosis of vascularized and nonvascularized intrahepatic lesions.

Our present results are in agreement with the original hypothesis that the use of a plasma label for scanning the hepatic blood pool will render more precise information about the size and boundaries of an abscess than the use of radiocolloids for scanning of the hepatic reticuloendothelial system. It seems that, on an average, the abscess itself contributes only to 23.9 per cent of the size of the concentration defect and that the area surrounding the lesion accounts for 76.1 per cent of the size of the defects depicted by liver scanning with radiocolloids (Fig. 2; 3; and 4).

The knowledge of the size and precise location of the lesions is of importance in deciding the type of therapy to be instituted. Medical treatment with antiamebic drugs will suffice if the lesion is small and there is no danger of rupture. However, if the lesion is large and located near the surface of the liver, its surgical drainage might be indicated to avoid its eventual rupture.

Scanning of the hepatic blood pool resulted in a more efficient definition of the actual size and number of abscesses than did liver scanning with radiocolloids. In 9 cases (7.2 per cent), multiple abscesses were masked by the failure of reticuloendothelial system to phagocytize the radiocolloid at the periphery of the other lesions, but they were perfectly defined by the imaging of the distribution of the hepatic blood pool (Fig. 2; and 4).

When the abscess is lodged near the lower surface of the liver, it is important to know the thickness of the nonfunctioning liver tissue separating the abscess from the abdominal cavity, as a thin layer of tissue may imply an eventual rupture of the abscess into this cavity. In most cases, this information is not obtained by radiocolloid scanning, but is easily secured by scanning with carrier-free, ionic In^{113m} (Fig. 4).

This procedure also proved to be useful in the study of abscesses of the left hepatic lobe, where liver tissue is thinner and may mask a concentration defect of a radiocolloid. In such cases, the lesion can be clearly depicted by circulating In^{113m} as a filling defect surrounded by the vascular bed of the liver and cardiac blood pool (Fig. 2; and 4).

Notwithstanding the fact that colloidal In^{113m} seems to be a better radiopharmaceutical than circulating In^{113m} in the study of small lesions, the process surrounding them may produce a larger filling defect than the actual abscess. In such cases, carrier-free, ionic In^{113m} proved to have a very poor resolution.

We may conclude that liver scanning with radiocolloids is the best routine procedure for the diagnosis and localization of amebic liver abscesses, but that in some special cases it should be complemented with a scintigraphic imaging of the distribution of the hepatic blood pool in order to gather more precise information about the actual size, shape, number and position of the abscesses.

SUMMARY

An amebic liver abscess consists of an area of necrosis caused by the implantation of trophozoites of the *Entamoeba histolytica*.

This necrotic area is surrounded by hyperemic liver tissue, evident by celiac axis angiography as a hypervascular region. This process interferes with the normal phagocytic activity of the reticuloendothelial tissue around the abscess creating a

bigger filling defect in the scans obtained with radiocolloids than the actual size of the lesion. Furthermore, when the abscess is located near the surface of the liver or in the left lobe, its boundaries are not precise in the scan image.

A comparative study of liver scanning with colloidal In^{113m} and scintigraphy of the hepatic blood pool with carrier-free, ionic In^{113m}, was carried out in 125 patients with proven hepatic amebic abscesses.

Carrier-free, ionic In^{113m} proved to be more precise in the imaging of the actual size, shape, number and position of the abscesses, but was less efficient than colloidal In^{113m} in depicting smaller lesions.

It is concluded that liver scanning with colloidal In^{113m} should be considered as the best routine procedure for the study and localization of amebic liver abscesses, but that in some special instances it should be complemented with a scintigraphic study of the distribution of the hepatic blood pool to gather more precise information about the actual size, shape, number and position of the abscesses.

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ARTERIOGRAPHIC FINDINGS OF FOCAL NODULAR HYPERPLASIA OF THE LIVER AND REVIEW OF THE LITERATURE*

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THE arteriographic features of 2 cases of focal nodular hyperplasia of the liver and its confusion with liver neoplasm and other abdominal pathology prompt this report. We have not found any similar reports in the radiologic literature, specifically about focal nodular hyperplasia.

This entity is well known to pathologists. Most frequently it is found in patients undergoing laparotomy for other reasons or at postmortem examination. The lesion has been called, or been confused with, a variety of other lesions, including adenoma, mixed adenoma, benign hepatoma, solitary hyperplastic nodule, focal cirrhosis, hamartoma, hamartomatous cholangiohepatoma, isolated nodule of regenerative hyperplasia, and focal nodular hyperplasia.[20] The difficulty in terminology appears to be from lack of agreement among pathologists as to the differentiation and definition of hamartomas, adenomas and hyperplasia. The standard for reference among most pathologists is probably Edmonson's monograph on liver tumors.[6] Histologically the lesion is similar to regenerating nodules in cirrhosis, except that the remaining liver in cases of focal nodular hyperplasia is normal.[2] The true nature of the abnormality is still uncertain. Some authors consider it a true neoplasm; others call it a congenital hamartoma; and yet others consider it to be a response to some injurious agent which is as yet unidentified.[3,6] The cells making up the nodules are not neoplastic and are identical to the hepatic cells seen in the regenerative nodules of cirrhosis. There are also bile duct proliferation, varying degrees of inflammation and vascular changes.

HISTORIC REVIEW

In 1884 Simmons[18] described a solitary hyperplastic nodule found in the left lobe of the liver in a woman at autopsy. The remainder of the liver was normal. He suggested in his discussion that the nodule may have resulted from a peculiar response of the liver to injury, but also considered the possibility of a congenital lesion. Hoffman[9] coined the term "benign hepatoma" in his report of a case and review of the literature up to 1942. He considered the possibility of malignant changes arising within these nodules. Begg and Berry[2] reviewed the literature from 1930 to 1953 and reported 4 additional cases, all of whom had surgery and were doing well after 1 to 3 years. They found 29 cases similar to the ones they reported and considered 28 of them incorrectly diagnosed as adenoma, benign hepatoma or hamartoma.

The autopsy records of the Mayo Clinic between 1922–1951 were reviewed by Benz and Baggenstoss.[3] They found 34 examples of the lesion which they termed "focal cirrhosis of the liver." The lesion was single in 29 cases, double in 4, and triple in 1. All cases of generalized cirrhosis were excluded. Small cavernous hemangiomas were found in addition to the regenerative nodules in 7 of these 34 cases (20.5 per cent). This is a greater incidence of cavernous hemangiomas than found in routine autopsies and greater than that found in Ishak's series of focal nodular hyperplasia.[10]

Edmonson[5] first used the term focal nodular hyperplasia in 1956. He discussed the differentiation from true adenomas of childhood, which are considered to be very

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rare. He feels that most liver adenomas of childhood, in the literature are actually instances of hyperplastic nodule or a slowly growing hepatoma. In another report Edmonson[6] speculates on the etiology and fate of the nodule if left alone. One patient remained in good health for 3 years and another for $7\frac{1}{2}$ years when only a biopsy was performed.

Wilson and MacGregor[21] in 1969 reported 4 cases of focal nodular hyperplasia, all of which were found in patients undergoing laparotomy for other conditions. One of these patients had only a biopsy and was doing well after $1\frac{1}{2}$ years. One of their cases had a liver scan with I^{131} rose begal. It showed an area of decreased function corresponding to the nodule which measured 7 cm. in diameter.

Whelan *et al.*[20] reported 4 cases, 1 of which is our Case 1. They propose an anomalous arteriolization of portions of the liver tissue with fibrotic and hyperplastic changes as the etiology. Two of their cases had follow-ups of 5 and $6\frac{1}{2}$ years respectively, after surgical resection.

In the literature there is a prevalence of cases in young adult females, but the spectrum includes children and patients in the eighth decade. Only scattered reports of abnormal liver function were noted. There is no distinctive pattern of presentation or symptomatology.

REPORT OF CASES

Case 1. J. B. was a 21 year old Caucasian female who was noted to have hepatomegaly in September 1967 during a prenatal examination in the second month of pregnancy. She was otherwise asymptomatic. Previous surgery included only an ovarian cystectomy and incidental appendectomy in March 1966. All liver function tests were normal. On September 18, 1967 she underwent an exploratory laparotomy and was found to have a large, lobulated, vascular tumor encompassing the entire left lobe of the liver. A biopsy taken during surgery was interpreted as focal nodular hyperplasia. The abdomen was closed and it was felt that definitive treatment could be delayed until completion of the pregnancy.

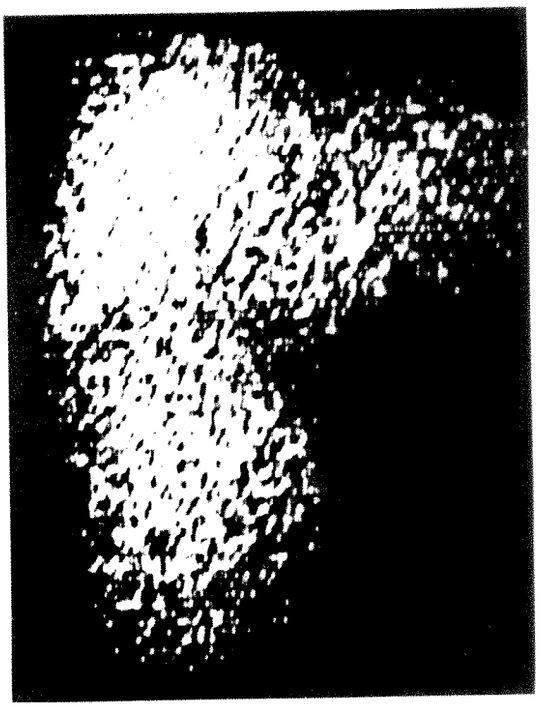


Fig. 1. Case 1. Au^{198} liver scan shows irregular decreased concentration in the markedly enlarged left lobe extending below the normal right lobe.

Following the operation she did well except for occasional right upper quadrant pain in the area of the incision. On February 6, 1968 she had a normal vaginal delivery of a viable child. She was admitted to Walter Reed General Hospital for further evaluation shortly after delivery. Physical examination at this time revealed the liver to be 3–4 fingerbreadths beneath the right costal margin with a diffuse but smooth edge. There was slight tenderness to deep palpation in the right upper quadrant. A bruit was heard directly over the xiphoid with radiation inferiorly. There was no splenomegaly and no abnormal venous pattern on the abdominal wall.

An Au^{198} liver scan (Fig. 1) was interpreted as showing irregular decreased concentration in both lobes of the liver with normal function only in the area just below the right hemidiaphragm. In retrospect, this area of normal function was the entire right lobe.

Percutaneous right femoral selective celiac arteriography showed enlarged common and left hepatic arteries and a normal caliber right hepatic artery. The left lobe was greatly enlarged with increased vascularity but no neo-

vascularity (Fig. 2, *A–C*). In the portal venous phase there were several dense, uniform, well circumscribed blushes which lasted through the end of filming—a period of 17 seconds. These findings were interpreted as a large cavernous hemangioma.

Surgical excision was undertaken because of the enlarging vascular mass, danger of rupture and increasing abdominal pain. During surgery excessive blood loss was encountered from the hepatic venous system; the patient became hypotensive and could not be revived.

Postmortem examination showed that the entire left lobe had been replaced by nodules of various sizes separated by strands of connective tissue. The left lobe weighed 1,280 grams. Histologic examination revealed characteristic findings of focal nodular hyperplasia. The right lobe was normal (Fig. 3, *A* and *B*).

CASE II. L. F. is a 28 year old Caucasian female who was first admitted to DeWitt Army Hospital in January 1972, for severe right upper quadrant pain suggestive of gallbladder disease. An exploratory laparotomy revealed the gallbladder to be normal, but a mass 2½ cm. in

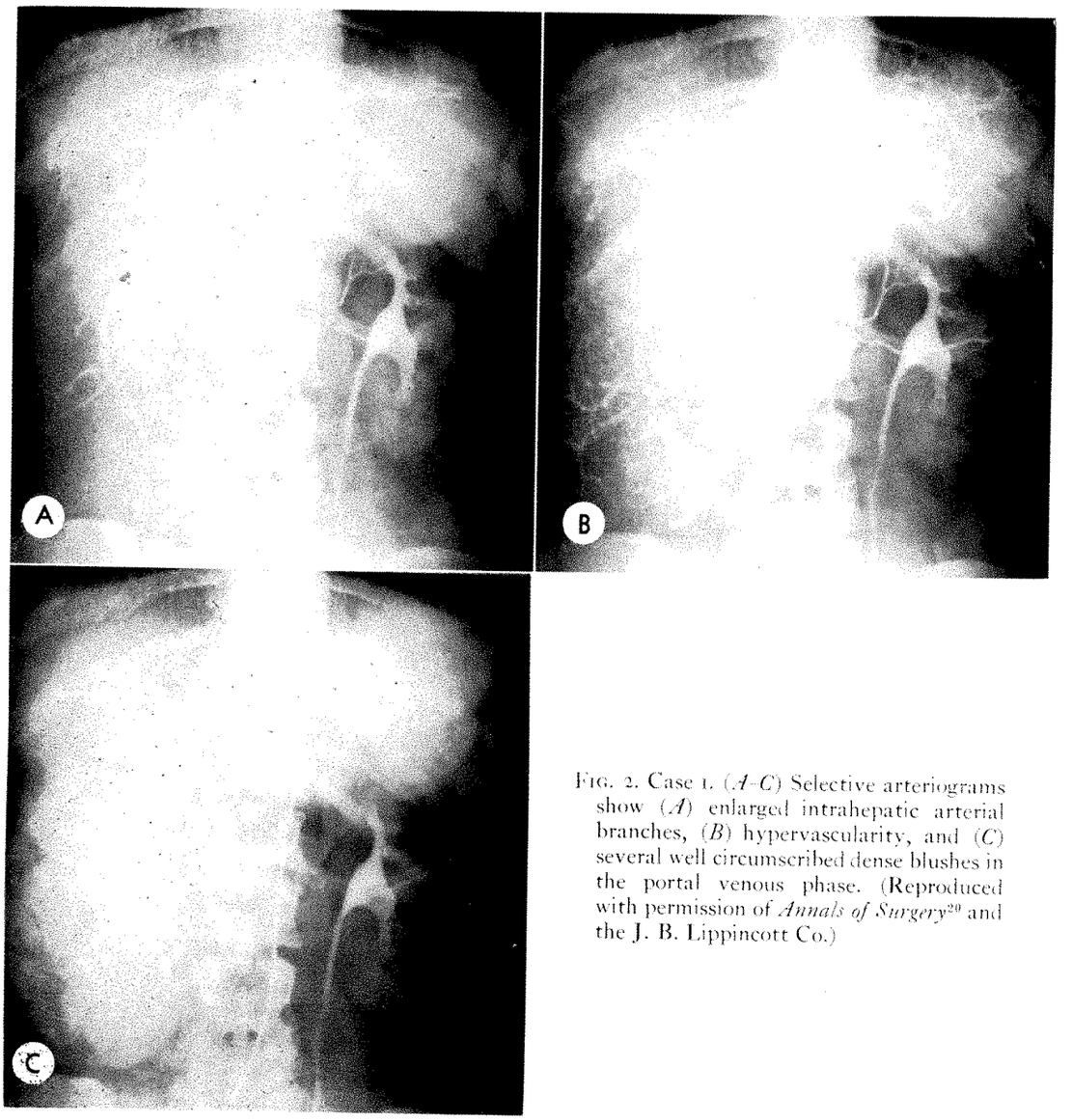


FIG. 2. Case I. (*A–C*) Selective arteriograms show (*A*) enlarged intrahepatic arterial branches, (*B*) hypervascularity, and (*C*) several well circumscribed dense blushes in the portal venous phase. (Reproduced with permission of *Annals of Surgery*[20] and the J. B. Lippincott Co.)

diameter was noted in the right lobe of the liver. Biopsy at this time revealed focal nodular hyperplasia.

Past medical history includes left salpingo-oophorectomy in 1969 and total hysterectomy in 1970 for dysfunctional uterine bleeding. She has mitral valve disease and is on digitalis.

Preoperative liver function tests were normal. Liver scans with Tc^{99m} sulfur colloid and I^{131} rose bengal were abnormal with concentration defects in the anterior inferior aspect of the right lobe (Fig. 4).

Following her initial surgery, selective celiac arteriography revealed normal major arterial branches and an area of increased vascularity without neovascularity in the inferior aspect of the right lobe. There was a uniform dense blush in the portal venous phase which lasted through the filming sequence of 17 seconds (Fig. 5, *A–C*).

Right hepatic lobectomy was performed because of persistent pain. The nodule measured 2.5 cm. in diameter and was located just below the anterior surface of the liver. The gross pathology was typical of focal nodular hyperplasia. The histology showed characteristic findings of focal nodular hyperplasia (Fig. 6). In addition there were 2 small cavernous hemangiomas, measuring 4 mm. in diameter, just below the surface, 5 cm. from the nodule.

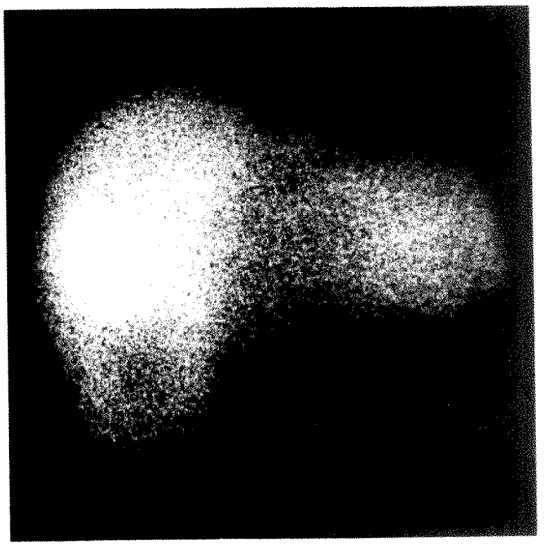


FIG. 4. Case II. Tc^{99m} sulfur colloid scan shows a well circumscribed concentration defect in the inferior aspect of the right lobe.

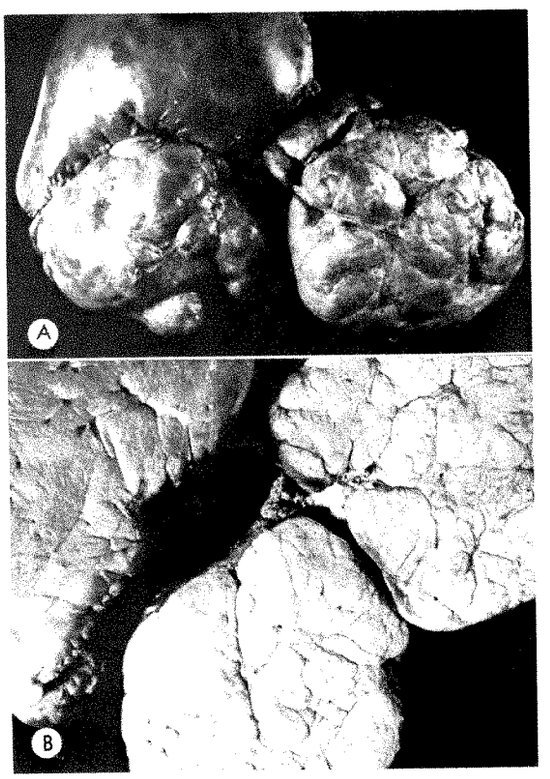


FIG. 3. Case I. (*A*) Gross specimen shows large lobulated mass adjacent to the normal right lobe. (*B*) Cut section shows division of masses into multiple pseudolobules by fibrous septa.

DISCUSSION

HISTOLOGY

The nodules of focal nodular hyperplasia vary greatly in both size and number. In the series reviewed by Benz and Baggenstoss[3] the size varied from 0.3 cm. to 8.5×17×18 cm. They are most commonly solitary, but may be multiple. They are more frequently found in the right lobe than the left. They are most often subcapsular in location, but more rarely may be found deep within the liver parenchyma. When pedunculated, torsion may result in vascular interference and severe pain.[7] The gross anatomic and histologic features of the lesions have been well described.[3,6,10] The lesions are well circumscribed, but do not have a true capsule. The sharp demarcation is the result of compression atrophy of surrounding parenchyma or a partial encirclement by a zone of connec-

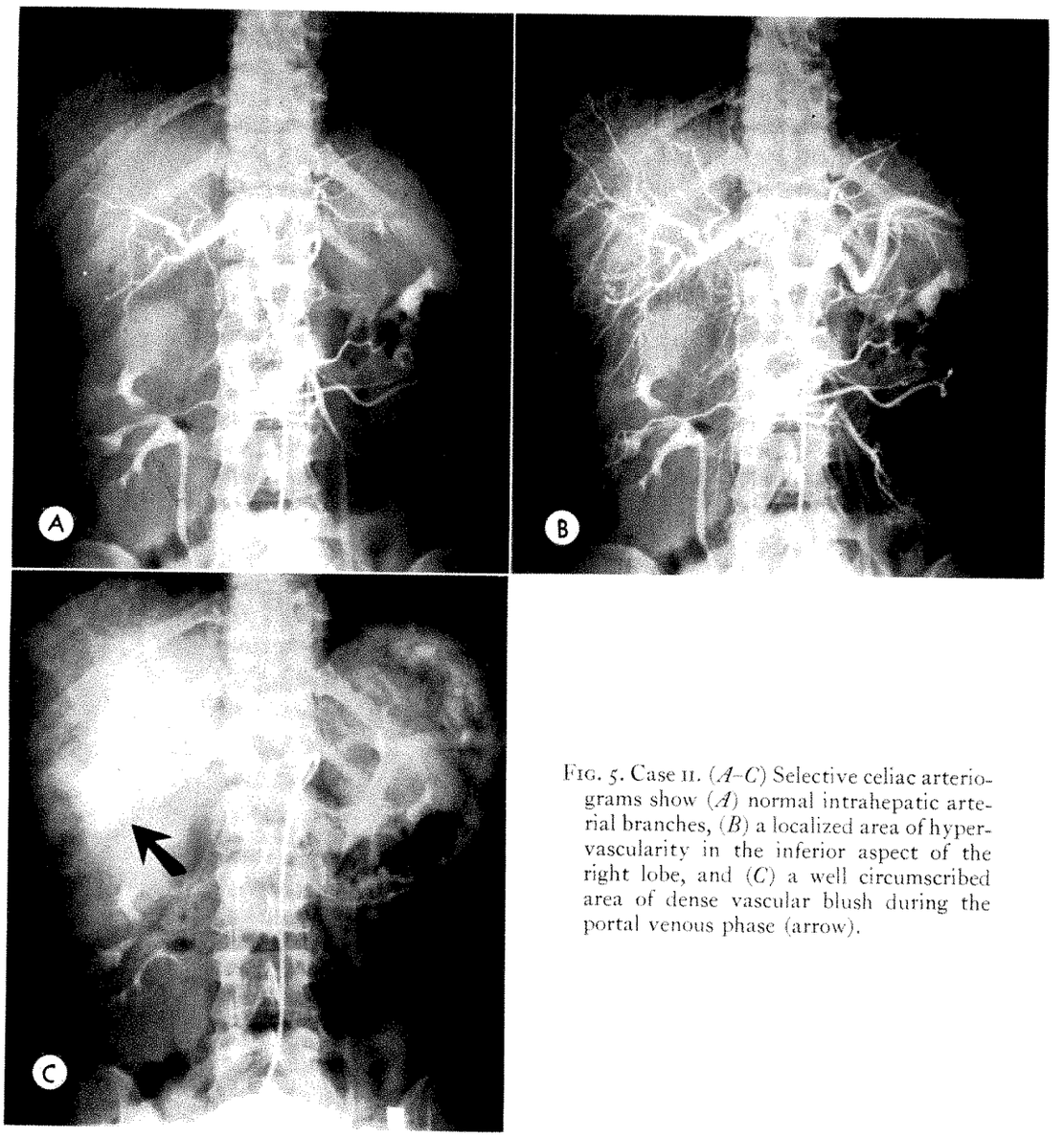


FIG. 5. Case II. (*A–C*) Selective celiac arteriograms show (*A*) normal intrahepatic arterial branches, (*B*) a localized area of hypervascularity in the inferior aspect of the right lobe, and (*C*) a well circumscribed area of dense vascular blush during the portal venous phase (arrow).

tive tissue. Viewed grossly, the large lesions have a central stellate scar with fibrous trabeculae extending radially to the periphery, dividing the mass into pseudolobules. The interlobular connective tissue contains many proliferating bile ducts, and lymphocytic infiltration is common. Histologically the parenchymal cells are normal regenerative liver cells and show no neoplastic changes. Edmonson[6] feels that these cells are arranged in a specific architectural framework, which sets it apart from the pattern seen in hyperplastic nodules of generalized cirrhosis. Histologically these are differentiated from hepatic adenoma by the lack of a true capsule, the presence of numerous proliferating bile ducts, and the stellate fibrous scar which is not seen in adenoma. Cases have been reported with increased cellular glycogen content. Although this is not a universal finding, it has been suggested

that the lesion may have some relation to the type of enzymatic defect seen in Von Gierke's disease.[8]

There is an abnormality of the vessels, both arteries and veins, characterized by intimal and medial hyperplasia. Sometimes the changes are so advanced, that one cannot determine which side of the circulation is affected. The lesion consists of spindle shaped cells, probably of smooth muscle origin, and sometimes fibroblasts.[6] Arteries may show fragmentation or reduplication of elastica. The nature of the vascular changes and its relation to the hyperplastic nodule are unclear. The possibility of an abnormal communication between the arterial and portal venous system has been suggested.[10] In several cases of focal nodule hyperplasia examined by Ishak,[10] in which the patient died in congestive heart failure, there was sparing of the nodules from the congestion and necrotic changes in the remainder of the liver. Were these areas protected from the high systemic venous pressure by connections to the portal system? Other evidence of portal system association comes from Sherlock *et al.*,[16] and Classen *et al.*,[4] whose cases of partial nodular transformation of the liver resemble focal nodular hyperplasia. Their cases all presented with esophageal varices and hemorrhage. There may be some correlation between the abnormal vessels and possible portal venous system involvement, and the pattern of late phase vascular blush in the arteriograms of our 2 patients.

Whelan *et al.*[20] consider the increased vascularity seen at arteriography to be etiologic. They cite animal experiments with surgical arterialization of the liver which produced similar vascular changes to those seen in focal nodular hyperplasia. Some animals have also shown fibrosis, inflammatory infiltrate and bile duct proliferation.

Evidence for arteriovenous shunting comes from the case of Aronsen *et al.*,[1] where a 2.6 liter per minute shunt was corrected to a 1.2 liter per minute shunt after resection of the lesion.

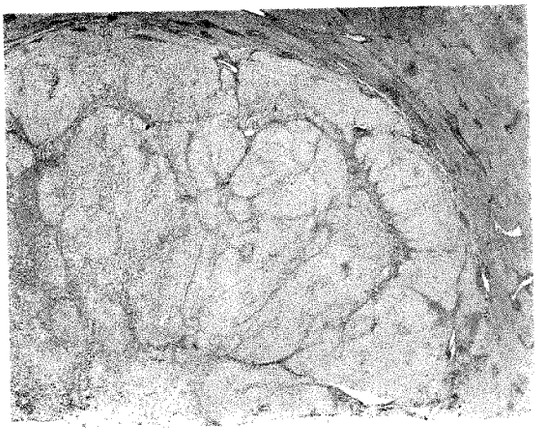


Fig. 6. Case II. Photomicrograph of a portion of the mass shows the pseudoencapsulation with compressed parenchyma and fibrous tissue, and the stellate fibrous septa within the lobules.

Isotopic Studies

Both of our cases had isotopic studies. Case I had an Au^{198} scan which showed mottled areas of decreased isotope concentration where the lesion was located. Case II had an I^{131} rose bengal study and a Tc^{99m} sulfur colloid study, both of which showed concentration defects in the area of the lesion. Case III of Whelan *et al.*[20] and Case IV of Wilson and MacGregor[21] also showed concentration defects with Au^{198} and I^{131} rose bengal scans. These findings indicated that there is abnormal polygonal and Kupffer cell function in the lesions.[17] In the regenerating nodules of cirrhosis, one may see either increased concentration,[19] normal concentration or decreased concentration[7] with Au^{198} scans. Scans of true liver cell adenomas show different uptake characteristics. In the case of Palubinskas *et al.*[12] there was a concentration defect with Au^{198}. The case of Sackett *et al.*[15] showed 2 masses, 1 of which was necrotic and gave concentration defects, and 1 of which was viable and showed normal concentration of both Tc^{99m} sulfur colloid and I^{131} rose bengal. Considering the difference in concentration of isotopes seen in cases of regenerating nodules of cirrhosis and true liver cell adenomas, it would not be surprising if a scan with increased concentration did occur. Perhaps the physiologic characteristics

change at different stages in the evolution of the lesion.

ARTERIOGRAPHIC FINDINGS AND DIFFERENTIAL DIAGNOSIS

The differential diagnoses of vascular masses in the liver include hepatoma, hepatoblastoma, hemangioma, hemangioendothelioma hamartoma, the vascular metastases of carcinoid, islet cell tumors, leiomyosarcoma, renal cell carcinoma,[14] adenoma,[12,15] regenerating nodules of cirrhosis,[7] and focal nodular hyperplasia. The characteristic arteriographic finding in focal nodular hyperplasia is increased vascularity with a well circumscribed blush that is more pronounced in the portal venous phase. Arteriographically, most hepatomas can be differentiated from focal nodular hyperplasia by the markedly enlarged intrahepatic arterial branches, the early arterial phase blush with irregular puddling of contrast material and the marked neovascularity.[14] In focal nodular hyperplasia, although there may be enlarged intrahepatic arterial branches and increased vascularity, there is no true neovascularity and the blush occurs late in the portal venous phase. The vascular metastasis of carcinoid, islet cell tumor, and renal cell carcinoma all show early arterial phase neovascularity and tumor blush.[14] Our Case 1 was confused with hemangioma, but in retrospect it did not show the orderly arrangement of discrete vascular spaces within the mass that was described by Pollard *et al.*[13] Hepatoblastoma is seen in children and arteriographically shows abnormal vessels and neovascularity with a dense homogeneous blush in the capillary phase, clearing in the venous phase.[4] The blush in our cases lasted well through the normal venous phase. True liver cell adenomas show neovascularity. In 1 case[12] there was an unusual reticular pattern of veins, and in another case[15] there was a dense blush in the venous phase. In our experience, true hamartomas of the liver give marked increase in vascularity without true neovascularity and there is no blush in the venous phase.

SUMMARY

The arteriographic and pathologic features of 2 cases of focal nodular hyperplasia of the liver are presented.

Focal nodular hyperplasia is characterized by increased vascularity without true neovascularity and a well circumscribed dense blush which becomes more intense in the portal venous phase.

Liver scans with I^{131} rose bengal, Au^{198} and Tc^{99m} sulfur colloid all showed concentration defects.

The varied presentation and benign nature of this entity are discussed.

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NONOPERATIVE RETAINED BILIARY TRACT STONE EXTRACTION*

A NEW ROENTGENOLOGIC TECHNIQUE

By H. JOACHIM BURHENNE, M.D.†
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RETAINED, overlooked, or forgotten stones present a common problem in bile duct surgery. Of the one-third of one million cholecystectomies done each year in the United States,[16] 20 to 40 per cent undergo common duct exploration. About 5 per cent or 5,000 patients require a second operation in order to remove retained biliary tract calculi (Table 1), although this figure increases without the use of routine operative cholangiography. The morbidity and mortality of the second surgical procedure is higher when compared to the primary operative intervention.

A new roentgenologic technique of nonoperative stone extraction in the ambulatory patient represents a significant improvement in postoperative medical management.

TABLE I

PERCENTAGE OF RETAINED STONES

Author	General and Review	Improvement with Routine Operative Cholangiography
Hicken and McAllister[15]	19	4.0
Shore[35]	17	3.0
Mixter *et al.*[27]	13	—
Parent and Peloquin[29]	10–20	3–5
Dowdy[9]	10	—
Jolly *et al.*[17]	8–28	6.6
Ferris and Sterling[13]	8–27	—
Kourias[18]	8–12	3.5
Bartlett and Dreyfuss[3]	6–11	—
Colcock and McManus[6]	5.0	—
Edmunds *et al.*[11]	3.5–27	3.5
Larson *et al.*[20]	3.1	—
Schulenburg[33,34]	—	1.4

DEVELOPMENT OF TECHNIQUE

Trans-T-tube catheterization using standard vascular catheters and guidewires has been used to dislodge sediment and blood clots in order to re-establish drainage.[24,36] Removal of the T-tube is indicated for the extraction of retained stones through the T-tube tract, with the tube left in place for 4 to 5 weeks after operation to establish a fibrous tract. Mondet[28] extracted stones through it as early as 1962 with a specially designed forceps. The same Mondet extraction forceps was successfully used by Mazzariello[25] even with larger stones after bouginage of the sinus tract. Magarey[21,22] preferred, for instrumentation, the Desjardins forceps and the Dormia* ureteral basket and catheter.

* V. Mueller, Chicago, Ill.

We started to use the Dormia ureteral basket in 1971, passing it either through the T-tube or, as described by Magarey, through a small arterial catheter.[5] Several case reports with this technique have appeared in the literature.[2,7,23,26,37]

We found the technique with small preshaped arterial catheters for placement of the stone basket rather time consuming, and the small tip of the relatively stiff arterial catheter was sometimes difficult to place and tented the wall of the biliary ducts. Sufficient contrast medium for continuous cholangiography was difficult to inject for continuous visualization of the retained stones. A second small arterial catheter was used initially for this purpose. These problems were corrected, and the

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† From the Department of Radiology, Children's Hospital and Adult Medical Center, San Francisco; and from the University of California San Francisco Medical School.

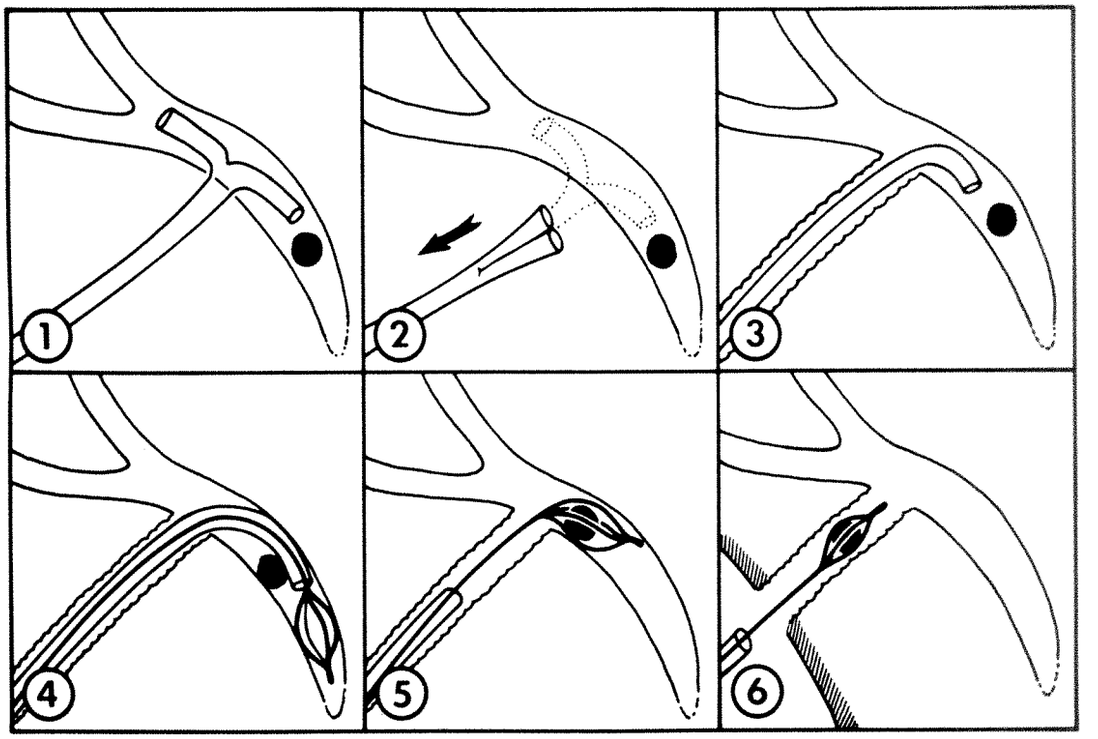


Fig. 1. *Technical steps for retained common duct stone extraction.*

1. Repeat T-tube cholangiogram is obtained on the day of stone extraction 4 to 5 weeks after choledochotomy
2. After the location of the retained stone has been ascertained, the T-tube is withdrawn
3. Using the sinus tract of the T-tube, the steerable catheter is guided into the bile duct, and its movable tip is advanced beyond the retained stone
4. The basket is inserted through the steerable catheter, the catheter is withdrawn and the basket is opened
5. The open basket is withdrawn in order to engage the stone. The basket is only retracted, never advanced, outside the enclosure of the steerable catheter
6. The stone is extracted through the drain tract.

procedure has been considerably shortened since we modified our instrumentation technique.

ROENTGENOLOGIC TECHNIQUE
(Fig. 1, *1–6*)

With the T-tube indwelling for at least 4 weeks after surgery, the ambulatory patient is returned to the x-ray department. T-tube cholangiograms are obtained for localization of retained stones. The patient is prepared and draped on the fluoroscopic table. Medication or anesthesia is not necessary. The T-tube is then extracted. This shows an average movement of the common duct by 1 or 2 cm.,[32] with the duct returning almost immediately to its previous position. This motion is absent in the presence of periductal adhesions.

A specially designed, polyethylene catheter† is then introduced through the T-tube tract. This steerable catheter permits remote control of the tip (Fig. 2, *A* and *B*) for easy passage through turns in the sinus tract and for direction of the tip into either the common hepatic or the common duct, depending on the position of the calculus. The catheter is 25 cm. in length. It has an external diameter of 4.3 mm. or No. 13 French and an internal diameter of 2.7 mm.

† Medi-Tech, Watertown, Mass.

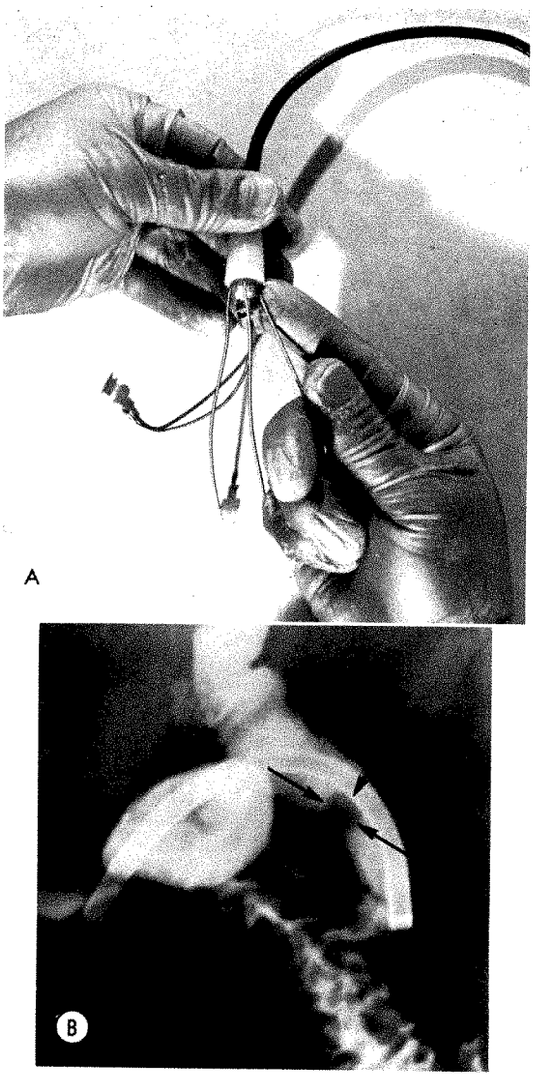


FIG. 2. Steerable catheter. (*A*) Traction from the outside on wires embedded in the wall of the catheter permits inside direction of the catheter. (*B*) The catheter is placed through the T-tube drain tract into the duct system, with its tip beyond the retained stone.

or No. 8 French, to permit passage of a variety of extraction instruments.

A side port is attached to the catheter for delivery of contrast material during the procedure. Intermittent contrast filling of the duct is obtained with a 300 cc. bottle of 30 per cent contrast medium, usually used for drip infusion pyelography.

After the large lumen steerable catheter has been placed with its tip beyond the biliary calculus, the Dormia basket is advanced through it, the basket is opened distally to the stone and the catheter is withdrawn leaving the basket in position (Fig. 3). The small point of the basket is never advanced outside the enclosure of the catheter.

Stones up to 10 mm. fit readily into the basket (Fig. 4). The basket is then closed and the stone engaged by advancing the basket sheath (Fig. 5). If larger stones are present, we have had good success with the use of a single or double sling passed through the catheter (Fig. 6, *A–C*; and 7).

If stones are fragmented and small fragments remain, a straight rubber catheter is placed, left in the common duct for several days, and control cholangiography is obtained (Fig. 9, *A* and *B*; and 10).

MATERIAL AND RESULTS

Twenty patients with retained bile duct stones after cholecystectomy and choledochotomy underwent roentgenologic instrumentation for stone extraction through the T-tube tract. The material is summarized in Table II.



FIG. 3. The catheter has been withdrawn and the stone extraction basket has been opened.

Case 9 (Fig. 8) was a failure because catheterization of the tortuous sinus tract was impossible. The T-tube had been placed in a midline incision. This patient underwent re-operation for stone removal.

Case 2 with 2 stones had 1 stone extracted. The other small stone slipped into the cystic duct remnant during instrumentation. The patient is asymptomatic 9 months after instrumentation.

Case 1 (Fig. 6, *A–C*) with a 3 cm. stone had the calculus extracted from the common duct, but it could not be pulled through the sinus tract. It was deposited in the proximal portion of the tract. The patient is asymptomatic on 10 month follow-up without abscess and with the sinus tract closed.

Case 4 (Fig. 9, *A* and *B*) had a 5 mm. stone which was fractured and then expelled into the duodenum. The follow-up intravenous cholangiogram is normal.

Case 6 had a 3 mm. defect, difficult to visualize during the procedure, apparently expelled into the duodenum. A straight rubber catheter was left in place for 1 week and the control cholangiogram showed no remaining filling defects.



Fig. 4. The stone basket is withdrawn several times until the stone is caught in the open basket.

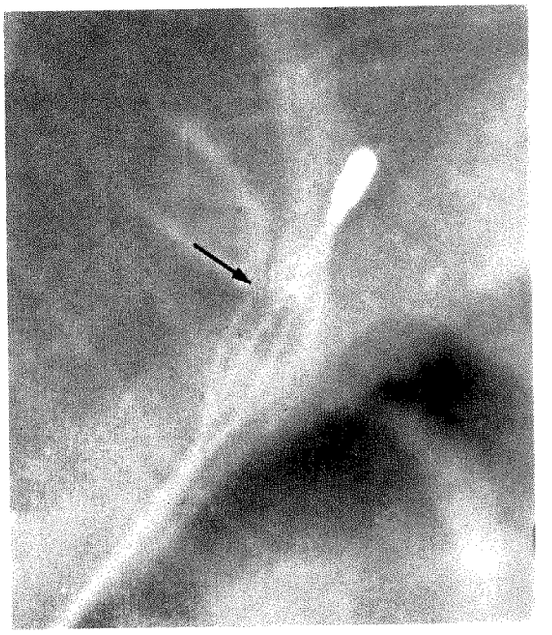


Fig. 5. The basket is closed around the stone by advancing the sheath.

Case 14 (Fig. 10) with an 18 mm. stone had a 14 mm. fragment extracted, the 4 mm. fragment passed into the duodenum. A straight French rubber catheter was introduced through the sinus tract into the common duct at the end of the procedure. The control cholangiogram 1 week later showed no remaining defects.

Fourteen patients with 20 stones had all of them completely extracted through the T-tube drain tract.

A second surgical intervention became unnecessary in all but 1 of the 20 patients. The sinus tracts healed and none of them have developed symptoms with follow-up ranging from 2 months to 12 months.

COMPLICATIONS

No complications occurred during instrumentation of 20 patients. No premedication and no local anesthetic was necessary. Some patients complained of pain during forceful contrast injection. Only dull pain sensation developed during instrumentation and only mild pain was experienced during extraction of a large stone through a small sinus tract.

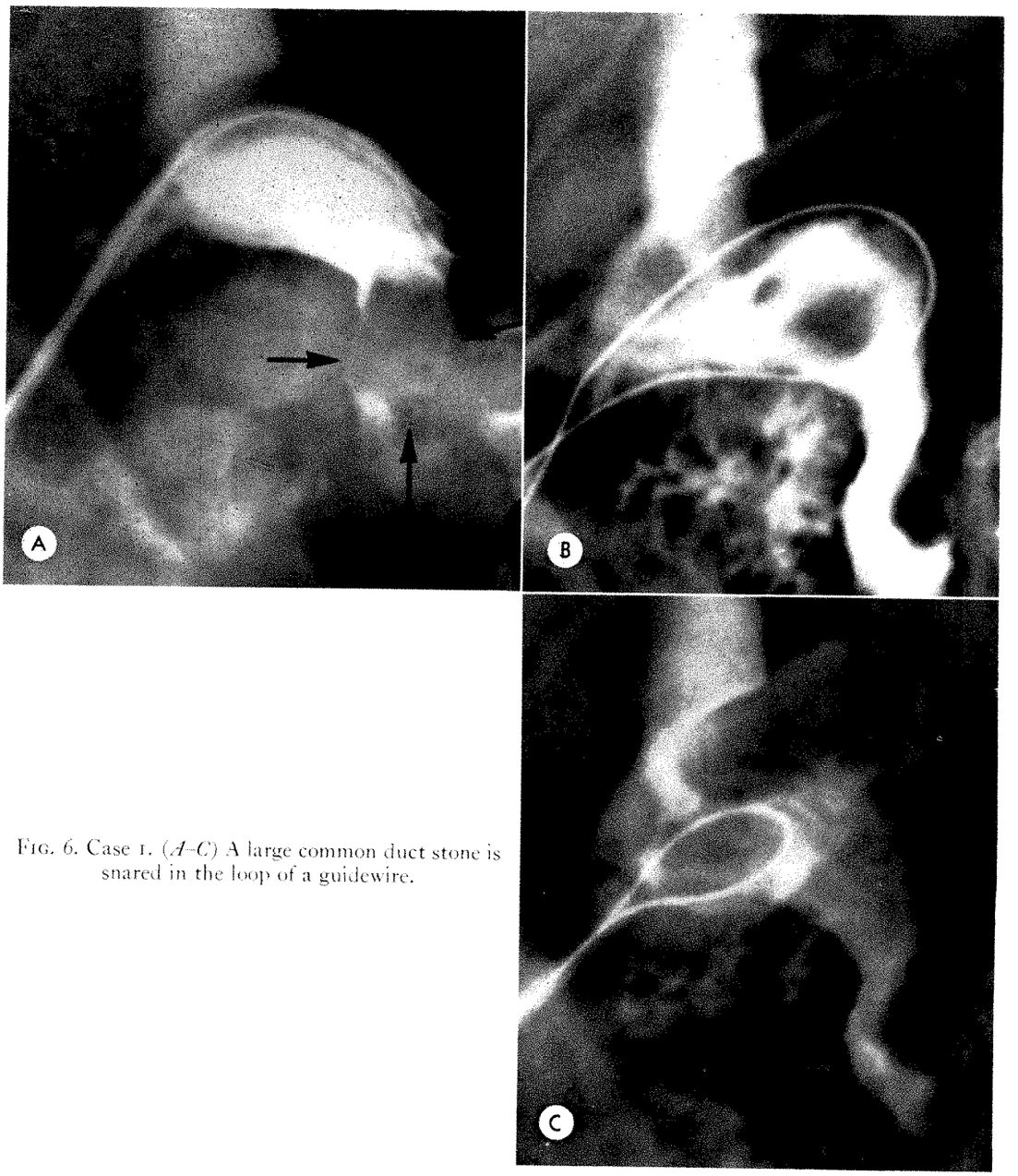


FIG. 6. Case 1. (*A–C*) A large common duct stone is snared in the loop of a guidewire.

Four of the 20 patients were placed on antibiotics by their referring surgeon, and a mild temperature increase occurred in 2 other patients on the first day after instrumentation.

The length of the procedure varied from 25 minutes for the patient in the room with $6\frac{1}{2}$ minutes of fluoroscopy time to $2\frac{1}{2}$ hours in the room and 45 minutes fluoroscopy time. The length of the procedure shortened as we gained experience. None of the last 10 patients were longer in the room than 45 minutes.

Radiation exposure was monitored in 2 patients. One patient with a total fluoroscopy time of 21 minutes received 7.5 r at

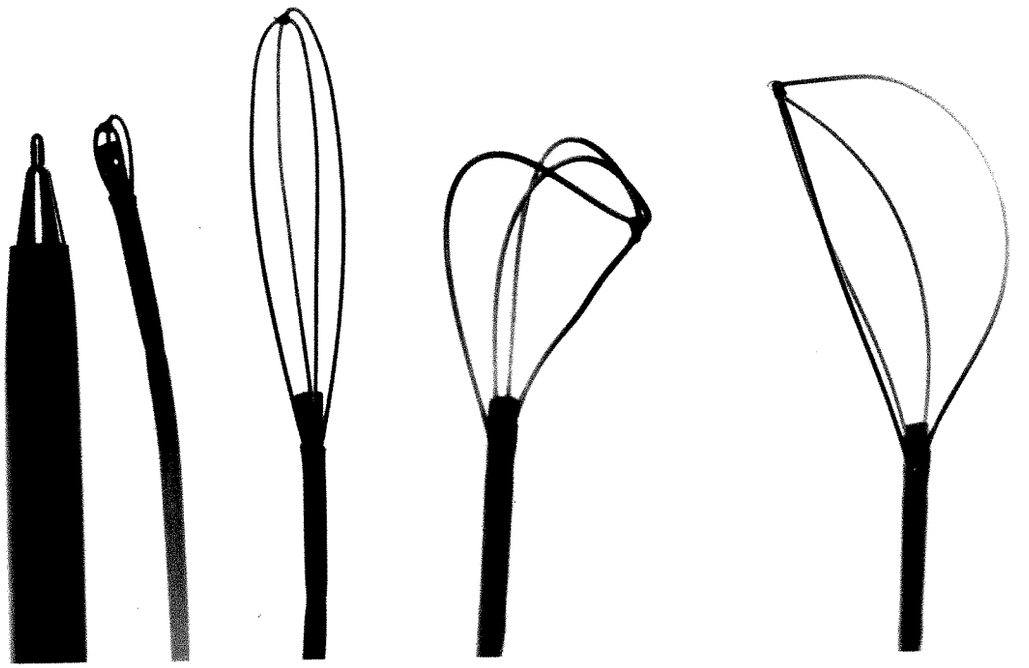


FIG. 7. A double snare forming a basket with 2 guidewires is placed through side holes in an arterial catheter. Traction on 1 of the 4 wire ends permits lateral manipulation distally to a retained stone.

the entry skin at the table top in the field and 120 mr on the anterior left chest wall outside the field. The roentgenologist received in the same case 40 mr at the dorsum of his right hand. A pocket dosimeter had been placed inside the rubber glove. A small shutter opening was used during the entire procedure with the roentgenologist's hands outside the field at all times. The roentgenologist received 27.0 mr during this procedure at the waist level outside his apron.

The radiation exposure dosimetry in the second case with 6½ minutes of fluoroscopy and cinefluorography time showed 2.5 r at the skin entry port at the table top for the patient and 80 mr on his left chest anteriorly. The roentgenologist received 27 mr on the back of his right hand and 4 mr on the outside of his apron at waist level.

DISCUSSION

The first technique employed in the non-

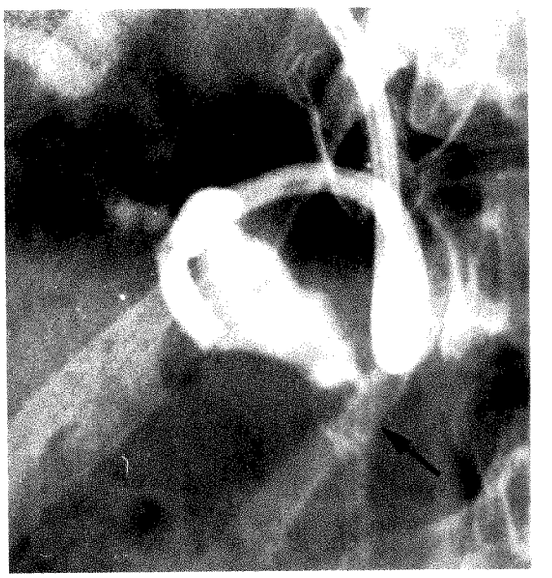


FIG. 8. Case 9. A second surgical procedure could not be prevented in this patient with retained common duct stone. The T-tube had been placed in the midline incision and the sinus tract was too tortuous for catheterization.



FIG. 9. Case 4. (*A*) The stone basket or (*B*) a small arterial catheter may be advanced through the distal common duct into the duodenum in order to expell small stones or stone fragments.

operative removal of retained biliary tract calculi was instillation of solvents such as ether or chloroform. Dissolution of stones was claimed by Pribram[30,31] as early as 1939. Dissolution of cholesterol stones by chenodeoxycholic acid was reported recently.[8] However, the vast majority of biliary tract stones contain little cholesterol. Eight of the 20 patients in our material underwent attempts of gallstone dissolution without success. Hospitalization for this procedure is costly and complications do occur.

Lamis *et al.*,[19] and Fennessy and You[12] reported successful expulsion of retained calculi in 3 cases. They employed a soft rubber catheter inserted through the tract of the removed T-tube. Combined with irrigation, the catheter was advanced into the duodenum and the stones passed (Fig. 9, *A* and *B*). Irrigation with oil[4] has also been reported.

The balloon-tipped Fogarty catheter has been used for stone extraction during choledochotomy.[1] We have tried this method postoperatively. The balloon was filled



FIG. 10. Case 14. If small fragments remain in the common duct after extraction, a straight French rubber catheter may be positioned and left in place for control studies at a later date.

Table II

SUMMARY OF CLINICAL MATERIAL

No.	Case	Sex	Age	Size and No. of Stones	Location	Result
1	R.G.	M	84	30 mm.	Common duct	Deposited in sinus tract; 10 mo. follow-up: sinus tract closed, no abscess
2	L.S.	F	26	4 mm. 4 mm.	Right hepatic duct Left hepatic duct	Right hepatic stone extracted. Left hepatic stone deposited in cystic duct remnant; asymptomatic on 9 mo. follow-up
3	G.U.	M	50	5 mm. 4 mm.	Common duct	Extracted
4	E.H.	F	74	5 mm.	Common hepatic duct	Fragmented and expelled into duodenum; asymptomatic on 9 mo. follow-up, intravenous cholangiogram normal
5	D.L.	F	34	5 mm.	Common duct	Extracted
6	A.L.	F	68	3 mm.	Proximal branch of T-tube	Expelled; T-tube cholangiogram 1 week later normal
7	J.B.	F	72	5 mm.	Left hepatic duct	Extracted
8	S.A.	F	78	11 mm.	Right hepatic duct	Extracted
9	T.W.	F	40	7 mm.	Common duct	Unsuccessful, tortuous sinus tract, could not be catheterized
10	M.F.	F	71	4 mm.	Common duct	Extracted
11	H.P.	F	38	5 mm. 6 mm.	Common duct	Extracted
12	B.R.	M	48	7 mm.	Common hepatic duct	Extracted
13	W.S.	F	62	9 mm.	Common duct	Extracted
14	J.K.	M	76	18 mm.	Common hepatic duct	A 14 mm. fragment extracted, a 4 mm. fragment passed; normal tube cholangiogram 1 week later
15	S.C.	F	68	8 mm.	Common duct	Extracted
16	M.F.	F	48	10 mm. 8 mm.	Common duct	Extracted
17	N.S.	F	76	10 mm. 6 mm.	Common duct	Extracted
18	L.F.	M	62	9 mm.	Common hepatic duct	Extracted
19	E.F.	F	72	6 mm.	Common duct	Extracted
20	A.L.	M	63	11 mm. 11 mm. 11 mm.	Common duct	Extracted

with contrast medium and placed distally to the calculus. The direction of extraction force to the side of the stone resulted in angulation, and the stone was wedged against the wall of the bile duct. We do not recommend this procedure. Eaton *et al.*,[10] and Henzel *et al.*[14] reported 5 cases of injury resulting with the use of the balloon catheter.

The Dormia basket was designed for the extraction of ureteral stones, but is ideally suited for biliary tract stones up to about 10 mm. size. Differently sized baskets are now available.* We constructed single (Fig. 6, *A–C*) or double (Fig. 7) snares for the extraction of larger stones. An .021 guide-

* Medi-Tech, Watertown, Mass.

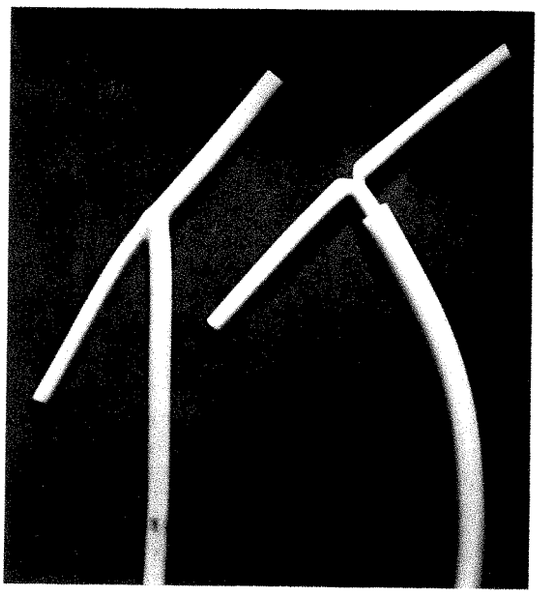


FIG. 11. A large caliber of the long arm of the T-tube is useful in stone extraction, because the diameter of the sinus tract limits the size of the calculus to be extracted. A larger catheter may be slipped over the T-tube in order to achieve this (*right*). T-tube catheters with an obtuse angle may be left in place after surgery if stones in hepatic radicals are known to remain. This will facilitate instrumentation postoperatively (*left*).

wire is well suited for this purpose. The 2 ends of the wire are maneuvered separately for positioning of the snare and in order to get behind the stone (Fig. 7). A single snare may slide off the stone during extraction, particularly if force is needed to pull a large stone through the sinus tract. If a stone is fragmented, we leave a soft, straight rubber catheter in place in the duct and repeat a control cholangiogram 1 week later to see if the small fragments were passed (Case 4, Fig. 9, *A* and *B*; and Case 14, Fig. 10).

If the stone is wedged distally in the common duct, the steerable tip of a smaller catheter is placed behind the stone and it is then moved to a more proximal position in the duct for extraction with the basket.

We have extracted stones up to 1.4 cm. in size through the sinus tract of a No. 16 French T-tube. We recommend that surgeons use T-tubes with a larger caliber of the long arm routinely after biliary tract surgery in order to facilitate subsequent instrumentation. A catheter of this type can be constructed readily in the surgical suite by slipping a large Foley catheter over the long branch of the T-tube after the ends of the Foley catheter are cut off (Fig. 11). The long branch of the T-tube should be placed in a right angle to the common duct, then through a lateral stab wound using a straight and short line to the skin. If a stone is seen in the hepatic radicals at operation and if it cannot be extracted at that time, a T-tube with an obtuse angle (Fig. 11) may be placed for roentgenologic catheter instrumentation after operation. Blind instrumentation during surgery in an attempt to extract stones in biliary radicals should be avoided if fluoroscopic control is not available. It may result in traumatic extravasation (Fig. 12).

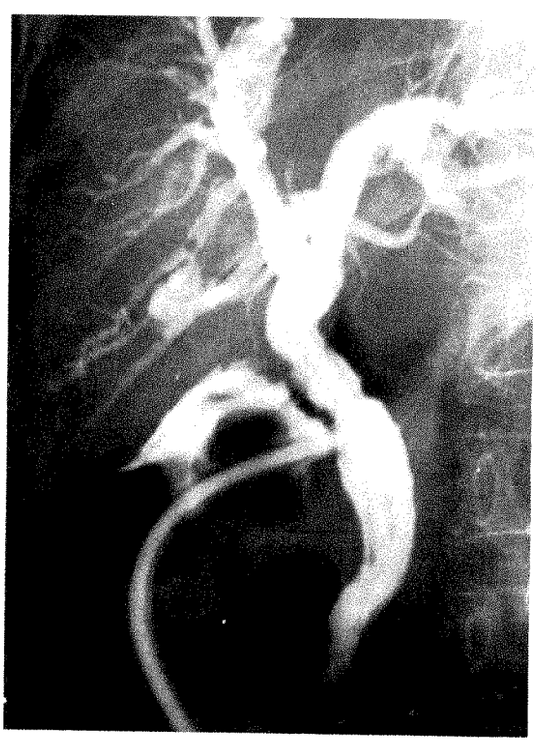


FIG. 12. Traumatic extravasation after attempt of operative instrumentation for small stone in hepatic radical. Extraction is best accomplished by nonoperative technique 4 weeks after surgery.

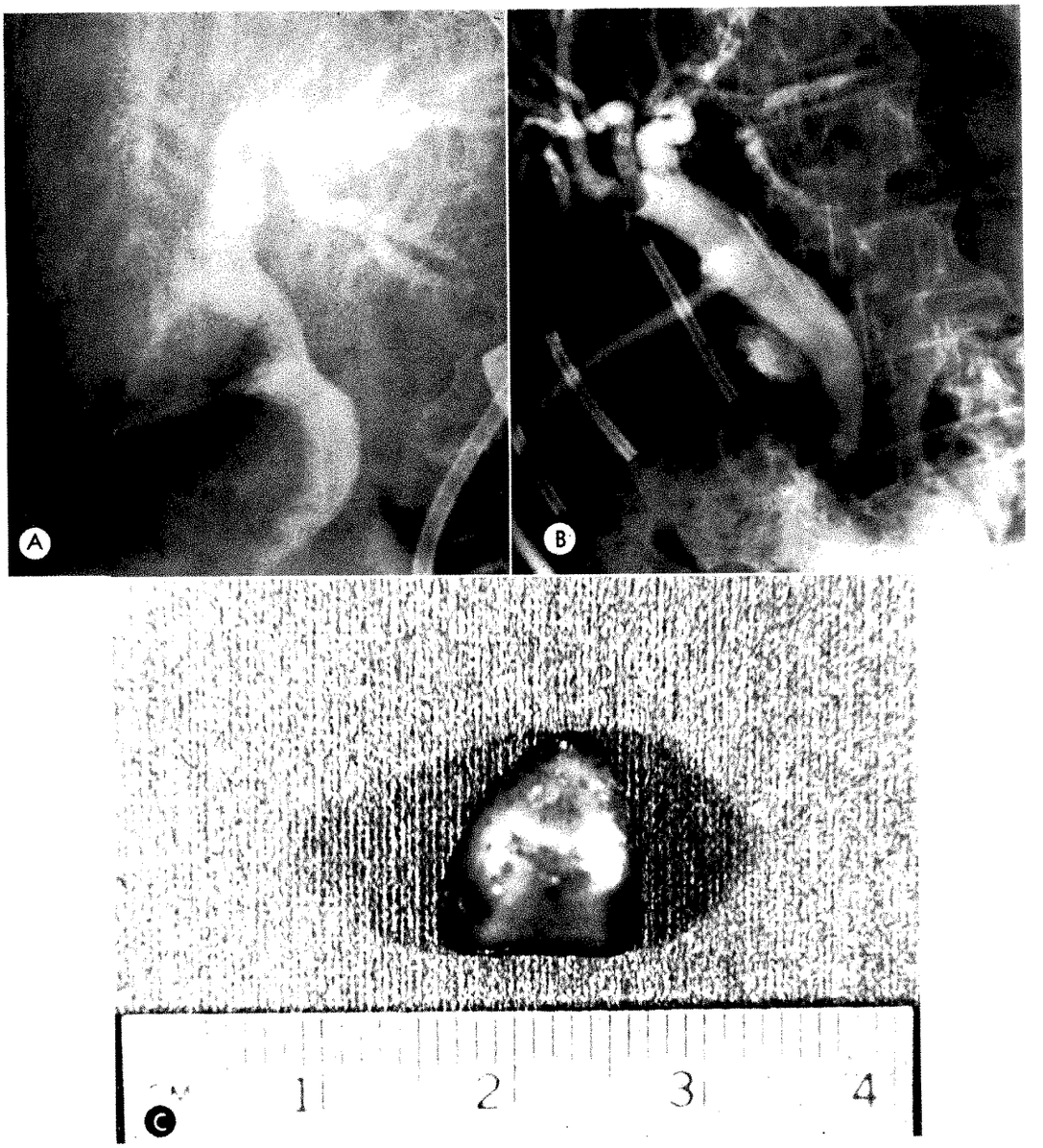


Fig. 13. Case 8. (*A*) This postcholedochotomy operative cholangiogram was called normal. The right main hepatic radical is amputated by a large remaining duct stone. (*B*) The postoperative T-tube cholangiogram shows the 11 mm. calculus clearly in the same patient. (*C*) The same stone was successfully extracted.

The stone is left in place and then extracted in the ambulatory patient by this roentgenographic method.

Small stones can present problems if they are smaller than 5 mm. They are difficult to visualize during the procedure (Case 6). Suction may be of use in these cases.

The entity of retained biliary duct stones will continue to be a common occurrence because of hepatic stones, silent stones, unreliability of duct palpation, 5 per cent falsely negative operative cholangiograms (Fig. 13, *A–C*), and because of the disuse of primary and secondary operative cholan-

giography.[17] But the answer to this problem is now available with the technique of nonoperative stone extraction. And even though some complications can be expected eventually, when compared to other therapeutic methods, the advantages of this roentgenologic technique are obvious.

SUMMARY

Our experience with 20 cases of nonoperative retained biliary tract stone extractions is presented.†

An improved instrumentation technique through a steerable catheter under roentgenologic control is described.

A second surgical intervention for stone removal became unnecessary in all but 1 of our 20 patients undergoing this new roentgenologic technique.

All 19 patients have remained asymptomatic after stone removal.

The technique was unsuccessful in 1 patient due to our inability to catheterize a tortuous T-tube drain tract.

Compared to re-operation or attempts of stone dissolution, extraction under roentgenologic control in the ambulatory patient is the method of choice for the treatment of retained biliary tract stones.

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I am grateful to my surgical colleagues for their help and encouragement.

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† Another 11 patients underwent successful stone extractions since the completion of this manuscript, bringing our total experience to 31 cases. As many as 4 retained stones were extracted in one patient. No complications occurred in any of the 31 cases.

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ROUTINE TOMOGRAPHY IN GALLBLADDER NONVISUALIZATION*

A METHOD FOR EXTENDED POSITIVE DIAGNOSIS

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WHEN one encounters a patient with a nonvisualized gallbladder in the course of an oral cholecystographic examination, how can one be certain that he or she has a diseased gallbladder? If an opacified common bile duct can be found, then this indirect conclusion becomes a positive diagnosis of an abnormal gallbladder. By adding tomography routinely to cases of gallbladder nonvisualization in oral cholecystography, we have dramatically increased the yield of positive diagnoses by demonstrating the common bile duct either alone or with an extremely poorly defined gallbladder (Fig. 1, *A* and *B*; and 7). In 103 of such patients, a secure diagnosis of biliary tract disease was made 75 times.

METHOD

Our approach to oral cholecystography is similar to that employed in many other institutions. The patient ingests 3 mg. of telepaque the afternoon prior to examination. The following morning, fluoroscopic spot roentgenograms are obtained if visualization is adequate (a lateral decubitus projection is added when necessary). If the opacity of the gallbladder is insufficient, a second dose of 3 mg. of telepaque is given, followed by a repeat examination the following morning. When visualization is still inadequate for fluoroscopic spot roentgenograms, the technician takes 2 roentgenograms, a 14×17 inch anteroposterior supine abdomen projection centered below the xyphoid process, and a 10×12 inch right posterior oblique projection of the right upper quadrant. When the gallbladder is still not seen, tomography of the right upper quadrant is automatically performed with the patient placed in the right posterior oblique position. A minimum of 3 films centered near the midline is obtained, with the radiologist in charge deciding when the study is to be terminated.

RESULTS

In 1,656 standard oral cholecystographic examinations over a 2 year period, the gallbladder could not be seen in conventional roentgenograms in 103 patients (6 per cent). In this group we were able to identify the common bile duct in the plain roentgenograms in 31 patients only (Fig. 1*A*). When tomography was included, we saw the common bile duct in an additional 31 patients. In several, the actual obstructing calculus was identified (Fig. 2*B*; and 3*B*), again primarily on the body section roentgenograms. Therefore, failure to identify the gallbladder in 62 patients meant cystic duct obstruction, the likeliest cause being a calculus impacted in the cystic duct or neck of the gallbladder. In a minority (13/103), the gallbladder itself was unexpectedly seen, albeit poorly opacified; 5 had nonopaque calculi (Fig. 7) and in 8 no calculi could be identified (Table 1). In 2 patients, calculi with faintly opaque rims were discovered in the common bile duct only on the tomographic studies (Fig. 6, *A* and *B*). We presume that these exhibited the rim opacification phenomenon described by Salzman *et al.*[5]

Of the 62 patients with cystic duct obstruction, 3 had previous cholecystectomies and 39 had subsequent removal of diseased gallbladders (Table II). Four patients in the second group of 13 with poor visualization had their gallbladders removed, with

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
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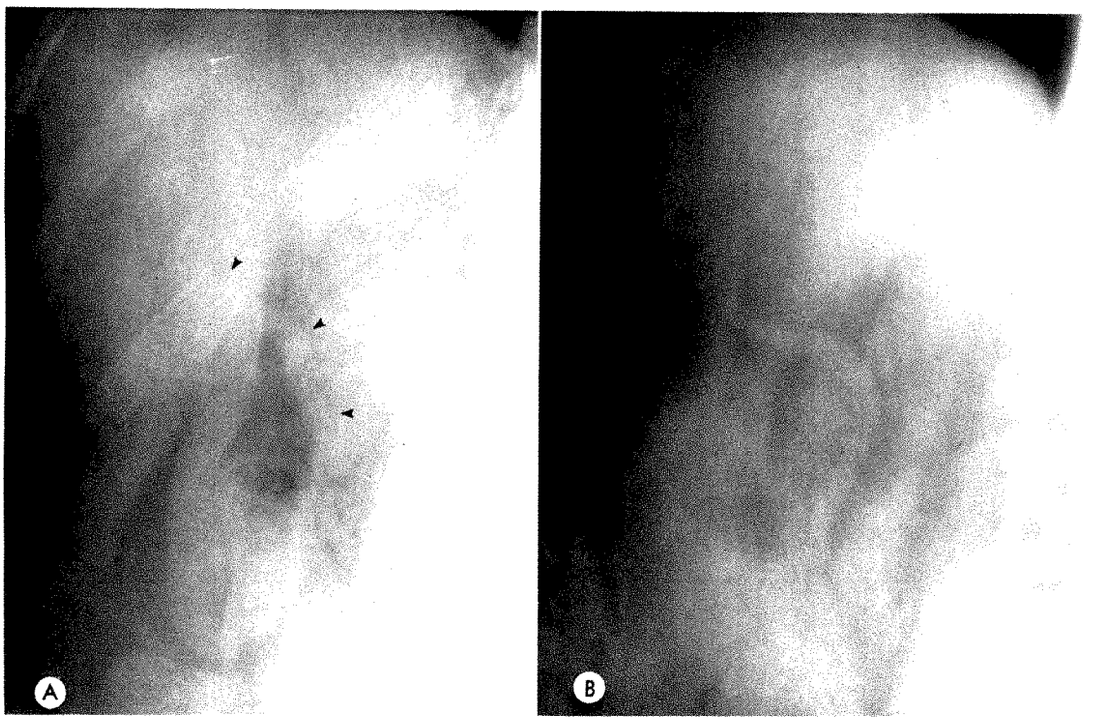


Fig. 1. (*A* and *B*) *Cystic Duct Obstruction.* L.S., a 69 year old white woman, underwent cholecystectomy for cholelithiasis and cholecystitis 1 day after this study was diagnosed as cystic duct obstruction. Tomogram (*B*) clearly reveals a normal common bile duct that can also be seen in the plain film roentgenogram (*A*). An oral cholecystography 1½ years earlier was reported as nonvisualization.

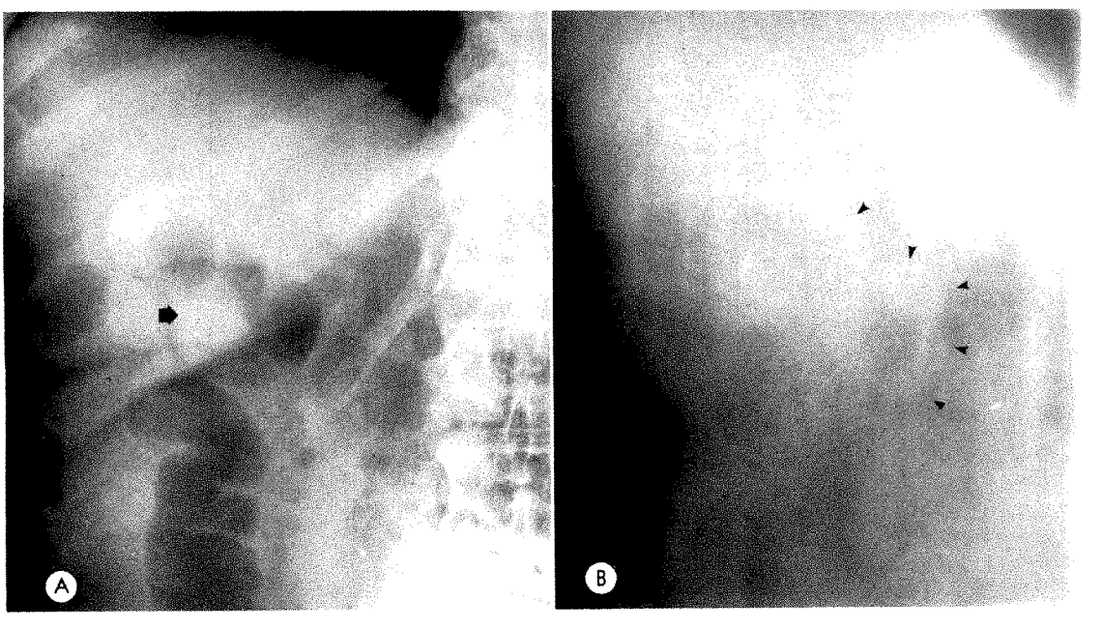


Fig. 2. (*A* and *B*) *Cystic Duct Obstruction Caused by Obstructing Calculus.* H.G., a 74 year old white male. Two small and 1 large calculi were removed from the gallbladder at surgery 3 weeks after this study. The largest stone is visible in the tomogram (*B*), adjacent to a normal sized common bile duct. In retrospect, it can barely be seen in the plain film roentgenogram (*A*) prior to tomography.

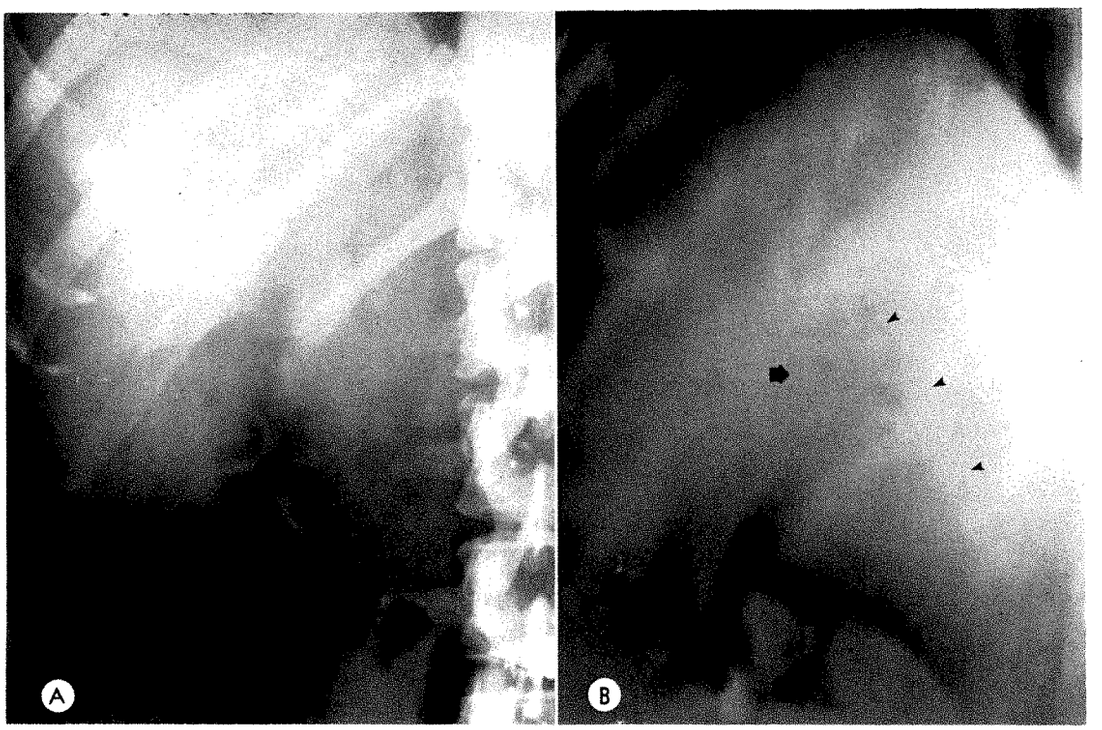


FIG. 3. (*A* and *B*) *Cystic Duct Obstruction Caused by Obstructing Calculus.* M.R., a 42 year old white female with no gallbladder visualization in the plain film roentgenogram (*A*). Tomogram (*B*) demonstrates a laminated calculus impacted in the neck of the gallbladder which prevents filling of the gallbladder by the opaque material. The faint common bile duct has a normal caliber. The diagnosis was confirmed by cholecystectomy 8 days later.

confirmation of the diagnosis. We have encountered no false positive diagnoses to date.

DISCUSSION

Nonvisualization of the gallbladder after successive daily doses occurs in less than 10 per cent of patients so studied.[2,4] Although many possible causes exist (including diarrhea, vomiting, biliary fistulae, as well as gallbladder disease), nevertheless more than 90 per cent of such patients will prove to have abnormal gallbladders surgically (Table III). Baker and Hodgson,[1] in their series of 1,207 studies, claim that 97 per cent of patients with nonvisualization

TABLE I

CHOLECYSTOGRAPHIC MATERIAL

Oral cholecystographies performed		1,656
Nonvisualized gallbladder		103
Plain film roentgenographic and tomographic findings in 103 cases		
1. Common duct visualized without gallbladder		
Plain film roentgenograms	31	
Tomograms	31	
Total		62
2. Poorly opacified gallbladder		
With calculi	5	
Without calculi	8	
Total		13
3. No helpful information		28

TABLE II

ADDITIONAL FINDINGS IN 62 PATIENTS WITH COMMON BILE DUCT VISUALIZATION

Cystic Duct Obstruction	
1. Common bile duct only	39
2. Calculus impacted in neck of gallbladder	8
3. Calculus impacted in cystic duct	2
4. Calculus in common bile duct	2*
5. Previous cholecystectomy	3*
6. Opaque stones (nonimpacting in nonopacified gallbladder)	9

* One patient in both groups.

Table III

PATIENTS WITHOUT GALLBLADDER OR DUCT VISUALIZATION

Total Number		28*
1. Gallbladder disease proven by other methods (surgery, intravenous cholangiography, etc.)	13	
2. Causes other than gallbladder disease (gastric outlet obstruction, fistula, liver disease, etc.)	9	
3. No answer	6	

* One patient had infectious hepatitis with nonvisualization of gallbladder or ducts. Two months later, oral cholecystography revealed a functioning gallbladder with calculi.

were abnormal. All gallbladders that were designated as poorly functioning were proven to be diseased. Since radiologists prefer positive diagnoses such as poorly functioning gallbladders to nonvisualization, many will proceed with intravenous cholangiography in the latter category. When one sees the common hepatic or bile ducts, either during intravenous or oral cholangiography and the gallbladder has been removed, one can safely conclude that the liver has adequate function to excrete the contrast medium into the bile ducts.

Wise[10] maintains that nonvisualization of the gallbladder in the presence of visible biliary ducts indicates cystic duct obstruction (due to calculus, fibrosis, inspissated bile, etc.) (Fig. 4*B*). Similarly, when the bile ducts can be seen following oral cholecystography, the same diagnosis is possible. Twiss *et al.*[9] described this situation as physiologic cholecystectomy or organic obstruction of the gallbladder due to impacted stones. In 3 such patients studied by their method of oral cholangiography, they visualized the bile ducts in two. Many have commented on seeing the bile ducts during routine cholecystography, but have felt that the visualization is not adequate or consistent enough in nonvisualization or

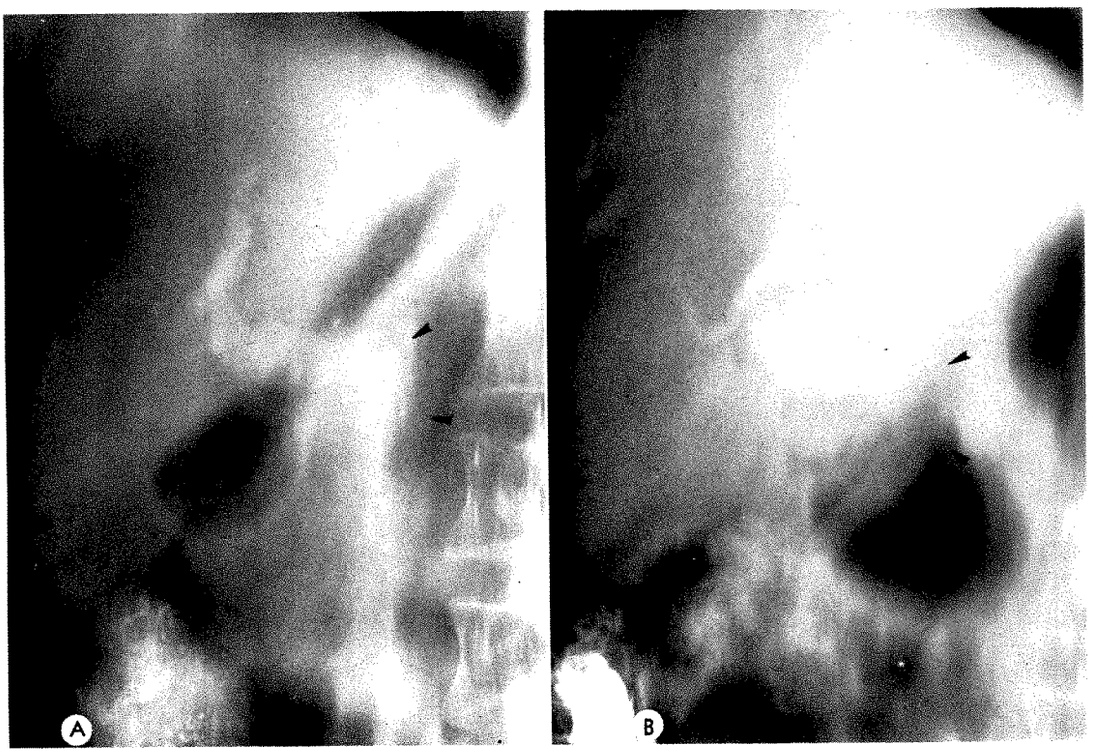


Fig. 4. (*A* and *B*) *Cystic and Common Bile Duct Obstruction.* E.D., a 76 year old white female. The well filled common bile duct in the oral study (*A*) suggests a distal obstruction. The intravenous cholangiogram (*B*) 4 days after the oral study shows slightly better the anomalous insertion of the cystic duct. No surgery was performed to date because of coexisting medical problems.



FIG. 5. *Postcholecystectomy Oral Cholangiogram.* S.T., a 69 year old white female. Routine oral cholecystography with tomography was performed for acute abdominal pain. Because of the significant dilatation and intrahepatic filling, a diagnosis of distal common duct obstruction in addition to cystic duct obstruction was made. A history of prior cholecystectomy was subsequently obtained.

postcholecystectomy to warrant its routine use, preferring intravenous cholangiography. Twiss and co-workers[9] claim a success rate of 70 per cent, and Shehadi[6] 50 per cent in seeing the bile ducts in postcholecystectomized patients by the respective technique of oral cholangiography (Fig. 5).

Stamatakos and Taber[3] actively sought the common bile duct in their series of 67 patients with nonvisualized gallbladders and found it in 48 patients (71 per cent). In all patients operated on, the diagnosis of gallbladder disease was confirmed. In the remaining 19 patients, 8 had gallbladder disease subsequently established, while 7

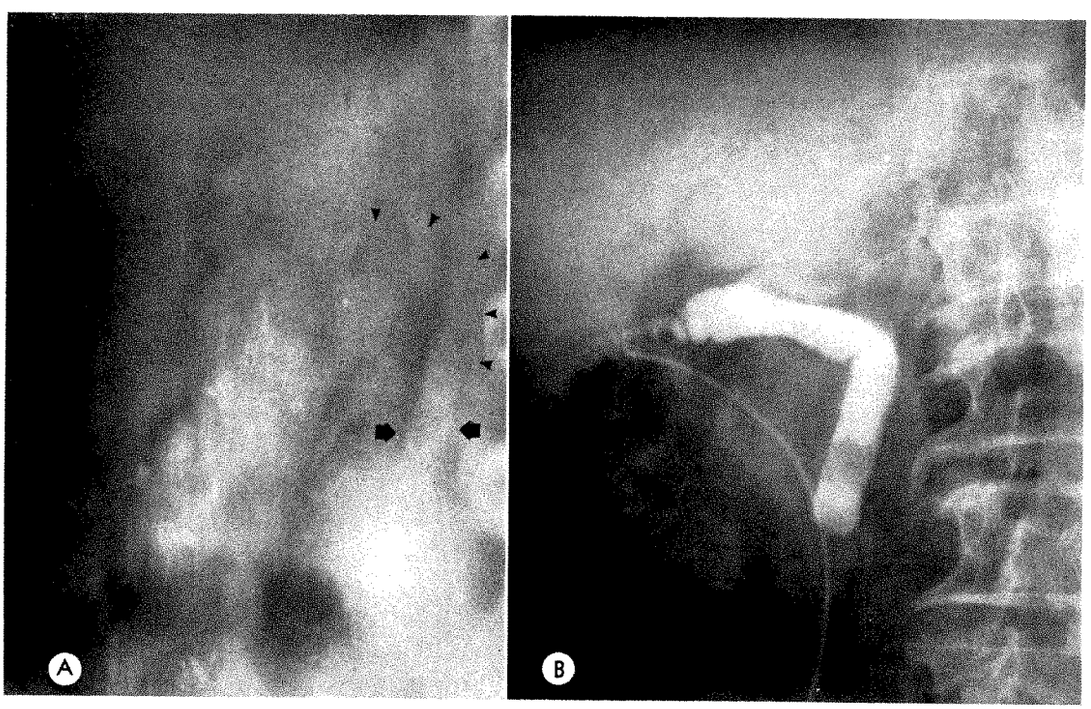


FIG. 6. (*A* and *B*) *Cystic Duct Obstruction and Common Duct Calculus.* F.F., an 80 year old white male. This patient had mild obstructive jaundice. Tomography after routine oral cholecystography (*A*) reveals cystic duct obstruction, a slightly dilated common bile duct (arrows), and a calculus with rim opacification (arrow). In the operative study (*B*), the calculus is confirmed as a negative defect.

had proven liver disease, and in 4 no explanation could be found.

Dann and associates[3] in a series of 200 consecutive patients with nonvisualized gallbladders found a visible common duct in 60 patients. Their conclusion was similar—gallbladder disease.

Sieniewicz and Kiss[7] could find only 59 patients with visible ducts alone out of 4,551 oral cholecystograms. They do not mention how many patients exhibited neither gallbladder nor duct opacification. Although they could not satisfactorily explain the mechanism of bile duct opacification, their conclusions were nevertheless similar—a visible common bile duct without identifiable gallbladder or calculi indicates gallbladder disease with calculi.

SUMMARY AND CONCLUSIONS

In 103 patients with nonvisualization of the gallbladder by conventional studies, a positive diagnosis of biliary tract disease was made in 75 when tomography was added. In 62 out of 75 the actual diagnosis was cystic duct obstruction. In the remaining 28 patients, at least ⅓ had causes other than the gallbladder as the reason for nonvisualization.

Without tomography, approximately ½ of the patients would have been diagnosed as having presumed gallbladder disease.

The need for intravenous cholangiography as a further diagnostic study has been significantly reduced.



FIG. 7. *Chronic Cholecystitis and Cholelithiasis.* E.M., a 73 year old white female. The slightly enlarged gallbladder containing several radiolucent calculi, visible on the tomogram, could not be seen in the plain film roentgenograms taken earlier the same day. The diagnosis was confirmed by cholecystectomy 1 week later.

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INTRAVENOUS CHOLANGIOGRAPHY*

AN EXPERIMENTAL EVALUATION OF SEVERAL CURRENTLY PROPOSED METHODS

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DESPITE the prevalence of intravenous cholangiography, no method of the procedure has been accepted universally. Methylglucamine iodipamide (MGI) is the only contrast medium currently approved for intravenous cholangiography. Yet, because of a lack of pharmacokinetic data about MGI, dispute exists regarding: the dose; the rate of administration; the use of glucose or sorbitol to stimulate contrast medium excretion; the optimum time after contrast medium injection for film exposure; and concomitant administration of oral biliary contrast agents with MGI.[1,7–9,15,20,22]

Cholangiography with both immediate injection and drip infusion is a current practice. The infusion technique reduces patient morbidity, but opinions differ whether opacification of bile is improved by this method. Various authors have reported that opacification of the biliary tract was improved when infusion cholangiography was employed,[1,2,4,5,8,12,16,20] but others have concluded that bile duct opacification is not significantly increased by the drip infusion technique.[3,7,22]

To resolve this controversy, we conducted a series of experiments in which concentration of biliary iodine after bolus injection was compared with that after drip infusion of MGI. Several currently proposed methods of cholangiography were evaluated experimentally.

MATERIAL AND METHOD

All studies were conducted on 3 unanesthetized, trained, adult dogs (17 to 24 kg.). They had been prepared previously by cholecystectomy and ligation of the accessory pancreatic duct. A duodenal fistula was produced by insertion of a Jones's cannula in the second portion of the duodenum.[10] Food was withheld from the dogs overnight. They were then placed upright in a sling and the common bile duct was catheterized through the duodenal fistula with a No. 190 polyethylene tube of 10 cm. length. Bile was collected by gravity drainage into graduated centrifuge tubes and divided into 15 minute samples. An intravenous infusion of 0.5 per cent sodium taurocholate* solution at a rate of 50 ml. per hour was maintained by a peristaltic infusion pump† throughout the experimental period.

Separate experiments were designed to compare concentration of biliary iodine after direct injection and after slow infusion of MGI. In all experiments, an initial 90 minute control period was maintained during which no contrast medium was administered. Each of the various experiments was performed at least once on each animal, so that each animal served as its own control. After administration of contrast medium, blood samples were obtained at 1, 5, 10, and 15 minutes, and every 15 minutes thereafter for the experimental period of 3 to 4 hours.

Samples of bile and blood were analyzed for iodine concentration by a fluorescent excitation technique with Am^{241}.[14] This

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‡ Trainee in Veterans Administration Radiology Training Program.

method has been shown to measure total iodine concentration to within ±2 per cent at levels of 40 μg./ml. to 60 mg./ml.

A. DIRECT CHOLANGIOGRAPHY

An intravenous injection of 0.6 ml./kg. of MGI was administered over a 2 minute period.

B. INFUSION CHOLANGIOGRAPHY

An infusion of 0.6 ml./kg. of MGI diluted to 100 ml. with 5 per cent dextrose and water was administered intravenously over a 30 minute period. Similar infusions were introduced with 25 per cent dextrose and water; normal saline; and 25 per cent sorbitol as the diluent.

C. INFUSION OF 2 BILIARY CONTRAST MEDIA

A constant infusion of 0.6 ml./kg./hour of MGI was maintained for 4 hours. After 105 minutes of the MGI infusion, 500 mg. of iopanoic acid solution was administered by direct intravenous injection over a 2 minute period.

RESULTS

A. DIRECT CHOLANGIOGRAPHY—

8 experiments (Fig. 1)

A maximum concentration of biliary iodine of 29.1 mg./ml. (±1.7 SEM) (standard error of the mean) was reached between 45 and 75 minutes after MGI injection. The mean concentration of iodine in blood ranged from 800 to 80 μg./ml. during the 4 hour experimental period. In the 15 minute period after the MGI injection, there was a rapid decrease in blood iodine concentration from 800 to 340 μg./ml. The serum iodine level then gradually decreased to 80 μg./ml. 4 hours after the injection. In the control period before the injection of MGI, the mean biliary flow rate was 4.5 ml./30 minutes (±0.7 SEM). After the injection of MGI, there was an immediate choleresis and the mean rate of biliary flow in the following 30 minute period was 13.8 ml. (±1.7 SEM). This difference was statistically significant ($p < 0.01$). An average of 64.6 per cent

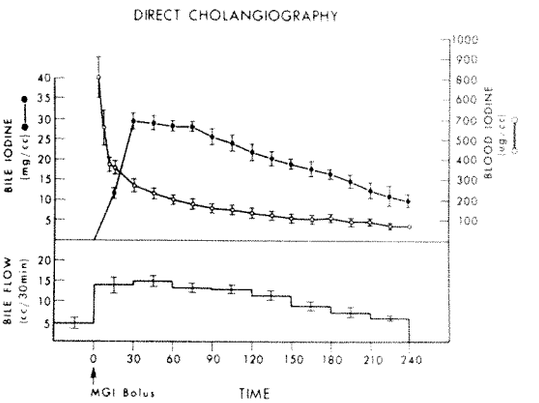


FIG. 1. Bile flow and concentration of iodine in bile and blood after a bolus injection of 0.6 ml./kg. of methylglucamine iodipamide (MGI).

(±2 SEM) of the administered iodine dose was recovered in the bile within 4 hours after the administration of the contrast medium.

B. INFUSION CHOLANGIOGRAPHY

a. *5% dextrose and water—4 experiments* (Fig. 2)

A maximum biliary iodine concentration of 32.7 mg./ml. (±2.0 SEM) was reached 45 minutes after infusion was begun and remained relatively constant for an additional 30 minute period. The mean level of iodine concentration in the blood decreased from 390 to 260 μg./ml. during the

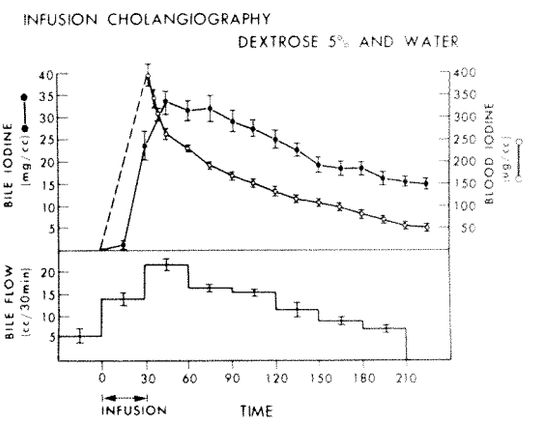


FIG. 2. Bile flow and concentration of iodine in bile and blood after infusion of 0.6 ml./kg. of MGI diluted to 100 ml. with dextrose 5% and water.

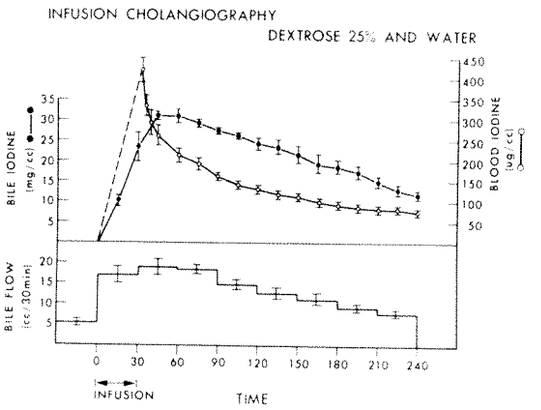


FIG. 3. Bile flow and concentration of iodine in blood and bile after infusion of 0.6 ml./kg. of MGI diluted to 100 ml. with dextrose 25% and water.

first 15 minutes after the completion of the infusion and then diminished more gradually over a 3 hour period to 60 μg./ml. following the completion of the MGI infusion. A significant ($p < 0.01$) increase in bile flow from 5.3 ml./30 minutes to 21.6 ml./30 minutes followed completion of the MGI infusion. Within $3\frac{1}{2}$ hours after the initiation of the infusion of contrast medium, 67 per cent (±3 SEM) of the administered dose of iodine was recovered in the bile.

b. *25% dextrose and water—4 experiments* (Fig. 3)

A maximum concentration of biliary iodine of 30.8 mg./ml. (±1.2 SEM) was obtained 45 minutes after the initiation of the MGI infusion. Serum iodine concentration decreased from 430 to 70 μg./ml. in the 4 hour experimental period. The time course of the decrease in iodine in the blood was similar to that after MGI infusion with 5% dextrose and water. In the 4 hours after the initiation of the infusion, 64 per cent (±4.1 SEM) of the administered iodine dose was recovered in the bile. After completion of the infusion, the biliary flow rate increased significantly ($p < 0.01$) from 5.3 ml./30 minutes to 18.7 ml./30 minutes.

c. *25% sorbitol solution—3 experiments* (Fig. 4)

The maximum concentration of biliary iodine was 32.5 mg./ml. (±0.9 SEM). This level was reached 60 minutes after the initiation of the infusion and remained relatively constant for an additional 30 minute period. The mean concentration of iodine in the blood ranged from 510 to 80 μg./ml. In the $3\frac{1}{2}$ hour experimental period, 57 per cent (±0.9 SEM) of the administered iodine was recovered in the bile. The time period of this gradual decrease was similar to that in the previous experiments. After completion of the MGI infusion, a significant increase in bile flow was again demonstrated ($p < 0.05$) from 7.7 to 20.7 ml./30 minutes.

d. *Normal saline—3 experiments* (Fig. 5)

A maximum concentration of biliary iodine of 29.0 mg./ml. (±1.4 SEM) was reached 45 minutes after the initiation of the infusion and remained stable for an additional 30 minute period. The levels of iodine in blood ranged from 420 to 80 μg./ml. and 58.6 per cent (±2.1 SEM) of the administered dose of iodine was recovered in the bile in 4 hours. Bile flow increased from 4.6 ml./30 minutes to 18.8

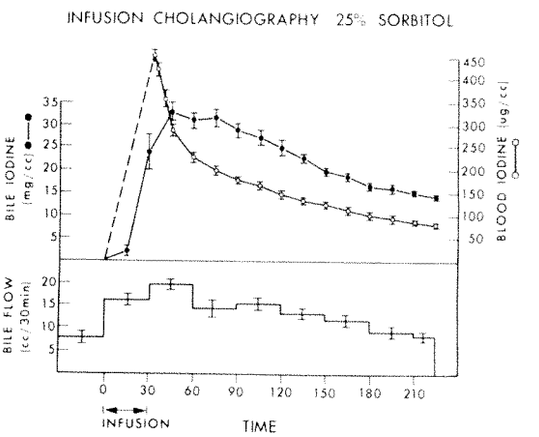


FIG. 4. Bile flow and iodine concentration in bile and blood after infusion of 0.6 ml./kg. of MGI diluted to 100 ml. with 25% sorbitol solution.

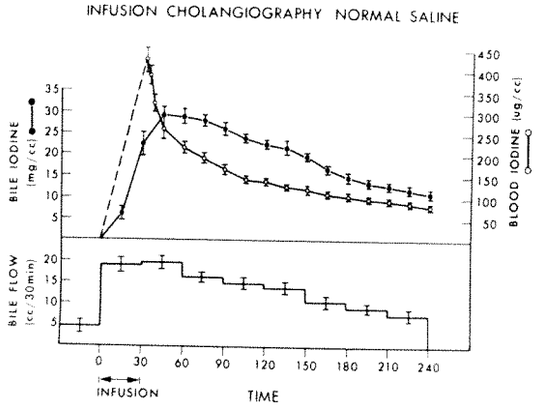


Fig. 5. Bile flow and concentration of iodine in bile and blood after infusion of 0.6 ml./kg. of MGI diluted to 100 ml. with normal saline.

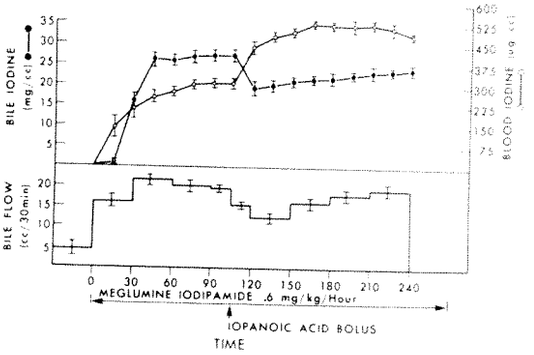


Fig. 6. Bile flow and iodine concentration in bile and blood during constant MGI infusion and after intravenous administration of 500 mg. of iopanoic acid.

ml./30 minutes after the administration of MGI ($p < 0.01$).

c. Infusion of 2 biliary contrast agents—*3 experiments* (Fig. 6)

Forty-five minutes after the initiation of a constant infusion of MGI, the concentration of biliary iodine stabilized at approximately 27 mg./ml. (±1.6 SEM). In the 15 minute period after the injection of 500 mg. of iopanoic acid,* the concentration of biliary iodine decreased to 19 mg./ml. (±1.1 SEM). The biliary iodine concentration was reduced despite an increase in blood iodine concentration from 300 to 440 μg./ml. Concentrations of iodine in bile then gradually increased to 24 mg./ml. (±0.8 SEM) 2 hours after the injection of iopanoic acid. There was a decrease in bile flow from 19.4 ml./30 minutes to 12.5 ml./30 minutes after injection of iopanoic acid. Biliary flow then gradually increased over the next 2 hours to 18 ml./30 minutes. A summary of our results is presented in Table 1.

* Sterling-Winthrop Research Institute, Rensselaer, N. Y.

Discussion

Theoretically, a slow intravenous infusion of MGI may allow a relative increase in the amount of MGI bound to serum proteins. This increase would decrease the unbound fraction of MGI and diminish the amount of free MGI available to be excreted by glomerular filtration in the kidney. Thus, more bound MGI would be available for uptake and excretion by the hepatocyte. If this hypothesis is correct a slow infusion of MGI may lead to higher concentrations, more prolonged significant levels of iodine in the bile, and an increase

Table I

Pharmacokinetics of Methylglucamine Iodipamide

	Maximum Bile Iodine	Time of Maximum Concentration	Time to T ½	Per Cent Recovered
Direct	29.1 (±1.7)	45 minutes	3¼ hours	64.6 (±2)
D5W	32.7 (±2.0)	45 minutes	3¼ hours	67.0 (±3)
D25W	30.8 (±1.2)	45 minutes	3½ hours	64.0 (±4.1)
Saline	29.0 (±1.4)	45 minutes	3¼ hours	58.6 (±2.1)
Sorbitol	32.5 (±0.9)	60 minutes	3 hours	57.0 (±0.9)

D5W = dextrose 5 per cent and water; D25W = dextrose 25 per cent and water.

in the total dose of contrast medium secreted into the bile.

In our studies, a slow infusion of MGI did not produce a statistically more significant increase in biliary iodine concentration ($p > 0.1$) than a direct bolus injection of the same dose of contrast medium. The time of maximum concentration of biliary iodine after injection of MGI and the percentage of the administered contrast medium recovered in the bile were not significantly different ($p > 0.1$). There was no prolongation of maximum biliary or blood iodine concentrations by the infusion method ($p > 0.1$).

The actual per cent of MGI bound to plasma proteins was not determined in these experiments; whether the protein bound fraction of MGI was actually increased by the infusion method is therefore not known. The degree of binding of contrast media to plasma proteins is probably only one factor that influences the excretory pathway of a particular contrast medium. Contrast agents that are relatively loosely bound to plasma proteins may be excreted in high concentrations in the bile, and some contrast media, tightly bound to plasma proteins, are excreted primarily in the kidney.[17] This observation behooves us to consider protein binding as a method of retaining contrast media in the plasma for transport to excretory sites rather than selecting which site of excretion will be preferred.

Several recent clinical reports have described increased opacity of the biliary tract after the administration of MGI and glucose, sorbitol, or hypertonic solution.[1,8,12,15,16,20,21] Theoretically, glucose and hypertonic solutions improve hepatic function by an increase in glycogen deposition and hepatic blood flow. Sorbitol has been stated to provide earlier and more prolonged opacification of the biliary tract by improving hepatocyte function.[15]

Our experiments did not substantiate any increase in concentration of biliary iodine, or prolongation of biliary clearance when MGI was infused with glucose, sorbitol, saline, or hypertonic glucose solutions. In addition, no statistically significant difference was noted between the mean maximum concentrations of biliary iodine and the time required to reach these concentrations after any of the tested methods of infusion cholangiography and the direct bolus technique. The most critical factor in iodipamide excretion may be speculated to be a specific transport mechanism of the hepatic cells. The degree to which this mechanism depends upon deposition of liver glycogen or hepatic blood flow remains to be determined.

The administration of a combination of contrast agents would provide increased concentrations of biliary iodine if each medium were excreted independently via noncompetitive pathways and no hepatic toxicity were produced by the combination of contrast media. Iopanoic acid is conjugated and excreted by the liver as a glucoronide,[11] whereas iodipamide is not excreted into the bile in a conjugated form.[6] Rather than an increase in concentration of biliary iodine, however, both the concentration of iodine in the bile and the biliary flow rates were depressed after concomitant administration of both agents.

The resultant decreased concentration of biliary iodine after administration of iopanoic acid and iodipamide is difficult to explain. The possibility that a 500 mg. bolus of iopanoic acid had a direct toxic effect upon the hepatocyte is not disproved, but in previous studies[13] similar doses of iopanoic acid were administered without toxicity. It has been suggested[18,19] that only a limited number of hepatic transport sites are available for excretion of drugs across the hepatic cell membrane. It may be that the 2 contrast agents compete for the sites on the transport mechanism. This competition may result in lower concentration of iodine in the bile if the more rapidly cleared contrast agent is displaced by that which is excreted more slowly. Our experiments were not designed to test this hypothesis.

Biliary flow was significantly increased

in all instances after the injection of MGI. Although this choleretic effect of MGI has been noted previously,[17] the mechanism of its production remains unclear. To what degree, if any, iodipamide acts as a stimulator of bile salt excretion or a substitute for bile salts also is not known. Nor is the degree to which iodipamide is secreted or concentrated by the ductal cell known. These compartmental kinetics from plasma to hepatocyte to bile are areas for further investigation.

SUMMARY

Direct and infusion cholangiography was compared in dogs. Biliary and blood iodine concentrations were measured and biliary flow rates recorded continuously.

The conclusions reached are:

1. maximum biliary iodine concentration is not increased by a slow infusion;

2. glucose, sorbitol, hypertonic glucose, saline and iopanoic acid caused no increase in biliary iodine concentration;

3. slow infusion failed to prolong biliary iodine levels;

4. slow infusion failed to cause an increase in the per cent of iodine dose recovered in the bile.

The clinical rationale for using drip infusion appears to be only the decreased morbidity in patients.

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EVALUATION OF RENAL FUNCTION FOLLOWING DOUBLE DOSE INFUSION INTRAVENOUS CHOLANGIOGRAPHY

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SLOW, gravitational drip infusion intravenous cholangiography, as compared to the more rapid direct injection with hand pressure, has been offered as a means of improving opacification of the bile ducts and as a method to minimize the acute dilutional changes which might occur in the vascular system.[11,18] Potentially, it is also a procedure which offers a decrease in the incidence of side effects with increased convenience in performing the examination. Furthermore, increasing the recommended dose of iodipamide methylglucamine 52%, (cholografin methylglucamine 52%), from 20 to 40 ml. has also been stated to result in better opacification.[4,9,17,18] In contraposition, others have felt that using larger doses of contrast material with the infusion technique provides only minimal improvement in opacification,[6] and may even produce slightly poorer visualization.[11] Experimental work in dogs has shown that the optimal iodipamide methylglucamine 52% dosage level is approximately 0.6 ml./kg. body weight, (or 312 mg. iodipamide/kg.; *e.g.*, approximately 40 ml. for a 70 kg. man), and doses greater than this do not produce significantly higher values of biliary iodine.[10]

Cholografin for drip infusion given intravenously to anesthetized and unanesthetized dogs, (at a rate of 8.3 or 16.6 mg. iodipamide/kg./min.), in total doses equivalent to or exceeding 510 mg. iodipamide/kg. depressed renal plasma flow, and in some cases, glomerular filtration.[24] The purpose of the authors is to report the results of monitoring of renal function, before and after infusion of 40 ml. of iodipamide methylglucamine 52%.

MATERIAL AND METHOD

All patients with known renal disease were excluded from the study. Ten patients were selected on the basis of having clinical findings requiring visualization of the biliary tract (Table 1). Of the 10 patients, the clinical diagnosis included choledocholithiasis, cholecystitis and/or cholelithiasis and pancreatitis. There were 7 females and 3 males, between the ages of 22 and 61, with an average of 38 years. The body weights varied between 50 and 85 kg., with an average of 69 kg. The height of the patients ranged from 152 to 177 cm., with an average of 162 cm. The body surface areas (BSA) ranged from 1.47 to 1.99 $M.^2$, with an average of 1.74 $M.^2$. All patients were on a normal or low residue diet the day before examination. Prior to the examination, the patients were maintained in a fasting state for approximately 8 hours. The bowel was prepared by means of cleansing enemas during the morning of the examination.

Forty ml. of iodipamide methylglucamine 52% diluted with normal saline to a total volume of 100 ml. was infused intravenously over a period of 30 minutes. Prior to injection, the contrast medium was warmed to body temperature. Iodipamide methylglucamine for intravenous cholangiography is supplied as a sterile, aqueous solution.* Each ml. contains 520 mg. of

* E. R. Squibb & Sons, Inc., Princeton, New Jersey 08540.

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TABLE I

RENAL HEMODYNAMICS

(Vital data on patients studied before and after intravenous dose of cholografin)

Patient	Diagnosis	Sex	Age (yr.)	Height (cm.)	Weight (kg.)	BSA ($M.^2$)	Serum Creatinine (mg./100 ml.)	Bilirubin (mg./100 ml.)	Dose of Iodine (mg./kg.)	Dose of Iodine (mg./1.73 $M.^2$)
1. G.R.	Choledocholithiasis	F	45	162	73	1.79	1.0	0.4	143	3,358
2. J.J.	Cholecystitis	F	22	157	75	1.77	0.8	0.5	139	3,396
3. R.B.	Cholelithiasis	M	61	172	85	1.99	0.8	0.3	122	3,021
4. M.M.	Cholelithiasis	F	53	167	79	1.89	1.0	0.7	132	3,181
5. A.R.	Cholecystitis	F	36	155	67	1.65	0.7	0.6	155	3,643
6. K.L.	Cholelithiasis	M	44	157	65.4	1.67	0.9	0.9	159	3,600
7. G.R.	Chronic Pancreatitis	M	25	177	57	1.72	0.8	0.6	183	3,495
8. J.C.	Cholelithiasis	F	45	152	80.4	1.80	0.8	0.3	129	3,340
9. W.M.	Cholecystitis	F	26	167	58	1.65	0.6	0.8	179	3,643
10. G.M.	Pancreatitis	F	25	152	50	1.47	0.6	0.7	208	4,074

BSA = body surface area.

iodipamide compound; however, the *bound* iodine content of the solution is 260 mg./ml., (10,400 mg./40 ml.). The total dose of *bound* iodine infused per patient varied from 122 to 208 mg./kg., with an average dose of 155 mg./kg. In relation to body surface area, the total dose of *bound* iodine varied from approximately 3,000 mg./1.73 $M.^2$ to 4,100 mg./1.73 $M.^2$, with an average of 3,500 mg./1.73 $M.^2$ (Table 1). All patients were observed for untoward reactions, such as flushing, nausea and skin rashes. The blood pressures and pulse rates were recorded at the start of the examination, at 10 minute intervals during the examination and up to one-half hour after the completion of the intravenous infusion of iodipamide methylglucamine. All of the patients studied had normal serum creatinine and bilirubin levels.

After taking anteroposterior and oblique roentgenograms for technique, further roentgenograms of the right upper quadrant were obtained every 20 minutes for 2 hours. Tomograms were secured at the time of optimal visualization of the common duct, and all tomograms were taken no later than 1 hour after the infusion. Opacification of the biliary tract on the roentgenograms was evaluated on a scale based on concentration of the opaque medium within the common duct as follows: excellent (optimum concentration of opaque medium); good (concentration of opaque medium diagnostic, but less than optimum quality); fair (concentration less than good diagnostic quality); and poor (faint visualization and nondiagnostic quality).

The following laboratory tests were performed either the day before or immediately before the intravenous infusion, and following the completion of the roentgen studies. Serum bilirubin; serum glutamic oxalacetic transaminase; alkaline phosphatase; serum creatinine; blood urea nitrogen; hemoglobin; hematocrit; white blood cell count and urinalysis were performed in the clinical laboratory of the Los Angeles County—University of Southern California Medical Center, using standard methods. Standard renal clearance methods were used to determine clearance of paraminohippuric acid, uric acid and inulin.[5,14,22,28] Osmolarity was measured by freezing point depression and urine pH was measured by pH meter. Renal plasma flow was calculated from the clearance of

TABLE II

CLEARANCE ml./min./1.73 M.²
(Average of three 20 min. periods of study)

Patient	Date of Study		Inulin*		Paramino-hippuric Acid†		Hematocrit		Renal Blood Flow	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1. G.R.	5/12	5/14	110	77	769	610	36	34	1202	924
2. J.J.	5/18	5/19	100	107	535	585	39	38	878	944
3. R.B.	6/3	6/4	102	100	427	439	40	36	712	686
4. M.L.M.	8/5	8/6	91	85	348	361	38	36	561	564
5. A.R.	9/8	9/10	89	130	416	603	33	33	621	900
6. K.L.	10/4	10/4	135	111	559	663	42.5	40	964	1105
7. G.R.	10/6	10/6	95	132	573	486	38	36	924	759
8. J.C.	10/13	10/13	93	85	503	368	36.5	38	786	594
9. W.M.	10/19	10/19	81	121	417	476	36	32	652	700
10. G.M.	10/27	10/27	133	143	828	808	36	33	1294	1206

Post values derived within 3 hr. of injection of cholografin except Patient 1.

Means and Standard Deviations in Normal Humans[22]

	Males	Females
* Inulin	124 ± 25.8/1.73 M.²	109 ± 13.5/1.73 M.²
† Paraminohippuric acid	654 ± 163/1.73 M.²	592 ± 153/1.73 M.²

paraminohippuric acid, assuming 95 per cent renal extraction. Renal blood flow was calculated by dividing renal plasma flow by (1-hematocrit).

RESULTS

There were no consistent changes in clearance of inulin or paraminohippuric acid in the 10 patients studied, and in all instances, their clearance remained within normal limits (Table II). Furthermore, there was no meaningful change in the calculated renal blood flow.

The uric acid clearance increased in all patients after the administration of the opaque medium. The magnitude of the percentage change was between 10 and 250 per cent (Table III). The increase in uric acid clearance did not correlate with any changes in inulin or paraminohippuric acid clearance. The urine pH and clearance of osmoles again did not correlate with the uric acid changes. The uric acid clearance generally increased in proportion to the increasing amounts of injected *bound* iodine/kg. (Fig. 1). The notable exceptions were Case 3 which had the smallest dose, *i.e.*, 122 mg. of *bound* iodine/kg. and demonstrated a large increase (8.6 mg. per cent) in uric acid clearance, and conversely Case 6 which showed little change with 159 mg. *bound* iodine/kg. A similar relationship was found when correlating with body surface areas.

Clearance of water decreased after iodipamide methylglucamine injection in all except 1 patient, even though there was no consistent change in clearance of osmoles. One patient excreted a concentrated urine (negative free water), after the study, but all others continued to excrete a dilute urine, albeit less dilute than before the study (Table III).

Sodium excretion rate did not change in any significant direction and similarly potassium excretion increased in some cases but decreased in others. There was no correlation between sodium and potassium excretion and the other parameters of renal function.

The serum bilirubin ranged from 0.4 to 0.9, with an average range of 0.6 mg./100 ml. before the examination, and did not change after the examination. There were

TABLE III

URIC ACID CLEARANCE, U pH, C osm, C H_2O, SODIUM AND POTASSIUM EXCRETION
(Before and after infusion cholangiography)

Patient	Plasma uric acid clearance/ml./min.				U pH		C osm		C H_2O		Sodium Excretion rate (μEq./min.)		Potassium Excretion rate (μEq./min.)	
	Pre	Post	Increase	% Increase	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1. G.R.	3.8	6.9	3.1	82	5	6	Not obtainable		Not obtainable		82	155	53	120
2. J.J.	4.3	5.9	1.6	37	5	5	Not obtainable		Not obtainable		215	283	21	29
3. R.B.	5.7	14.3	8.6	150	5	6	3.24	3.24	+ 3.27	+ 7.59	71	27	88	60
4. M.L.M.	3.8	4.4	0.5	16	6	5	2.65	2.51	+ 6.35	+ 6.24	81	76	61	29
5. A.R.	4.2	13.0	8.8	21	5	5	1.97	3.30	+ 6.37	− 1.49	105	285	31	47
6. K.L.	8.0	8.8	0.8	10	5	5	3.79	3.22	+13.52	+10.13	64	101	58	71
7. G.R.	5.9	13.0	7.1	112	6	5	2.50	2.52	+ 5.79	+ 5.17	53	49	88	56
8. J.C.	7.4	8.8	1.4	20	5	5	4.81	4.02	+11.81	+ 0.47	187	199	105	116
9. W.M.	7.8	27.0	19.2	250	5	5	2.11	2.60	+10.64	+ 5.76	92	126	25	47
10. G.M.	15.8	37.0	22.8	132	6	6	2.73	2.76	+11.05	+ 4.40	101	139	32	52

no meaningful changes in the serum glutamic oxalacetic transaminase, alkaline phosphatase, serum creatinine, blood urea nitrogen, hemoglobin, hematocrit, white blood cell count, urine specific gravity, albumin, sugar and microscopic examination.

No important side effects occurred, except for nausea and vomiting in 2 patients. The blood pressures and pulse rates did not change remarkably.

The roentgenograms of 6 of the patients showed excellent opacification of the biliary ducts, 2 showed good opacification, 1 showed fair opacification and 1 showed poor opacification.

DISCUSSION

The slow, intravenous infusion of 40 ml. of iodipamide methylglucamine was not associated with any discernible clinical side effects, and resulted in good or excellent opacification of the biliary ducts in 8 out of 10 patients. In addition, there were no changes in the formed elements of blood, in liver function, nor were there changes indicative of renal damage.

However, renal function was altered in several aspects. Uricosuria invariably followed the intravenous injection of iodipamide methylglucamine (Fig. 2). Others have reported a similar effect following intravenous cholangiography with iodipamide methylglucamine.[19] Furthermore, it is well known that weak aromatic organic acids, which characterize drugs used in intravenous pyelography and angiography, may also cause uricosuria.[12] It has been suggested that the increase in uric acid excretion after radiopaque media might account for an occasional case of renal failure. However, when such cases are analyzed, each is described as undergoing an acute reaction such as sudden collapse and hypotension.

In the present cases studied, there were no changes in renal blood flow or in glomerular filtration rate. In addition, there were

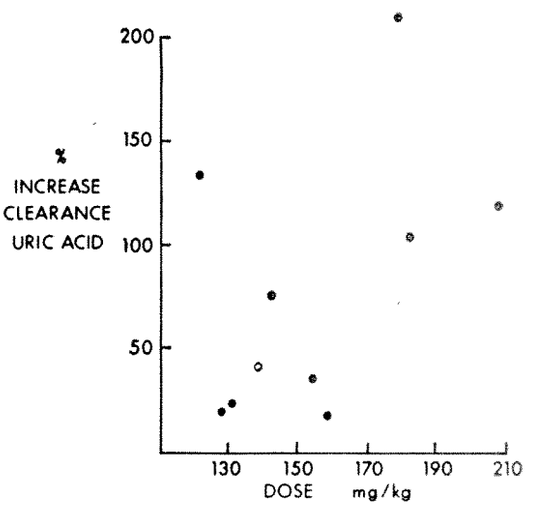


FIG. 1. Relationship between the change in uric acid clearance and injected *bound* iodine per kilogram.

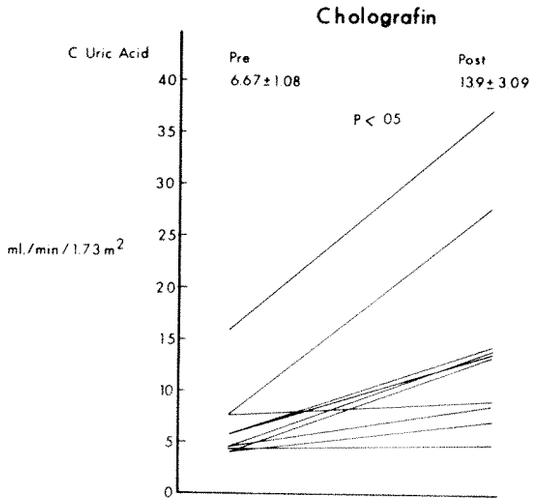


FIG. 2. Changes in uric acid clearance before and after cholografin injection. (Each line represents 1 patient; mean and SEM values are shown by the numerals at the top of the figure.)

no changes in osmolal clearance which could theoretically cause uricosuria.[21] The fact that there was no consistent change in monovalent electrolyte excretion is against the hypothesis that volume expansion was a factor.[26] Others have suggested that uricosuria is due to increased secretion of uric acid, stimulated by iodipamide methylglucamine, since the increase in uric acid clearance can be blocked by pyrazinamide.[26] Our studies do not include data which bear on this possibility, but recent evidence would cast doubt on the adequacy of pyrazinamide blockage as an agent which solely blocks secretion.[8]

Iodipamide methylglucamine is primarily excreted by the liver in humans, yet up to 19 per cent of an injected dose may appear in the urine.[7] In the dog, only that small percentage of iodipamide methylglucamine unbound to protein is filtered and excreted in the urine. The rabbit, however, can apparently secrete iodipamide methylglucamine by the renal tubule.[3] The uricosuric effect observed in the present study would indicate that the mechanism involved is extremely dependent on dose (Fig. 1). There is a good correlation of the dose of iodipamide methylglucamine per kg. and the clearance of uric acid. This finding may reflect an increased unbound fraction being delivered to tubular sites by filtration, where it could either block reabsorption or stimulate secretion of uric acid.

Another interesting finding in this study is the fall in free water clearance after intravenous injection of iodipamide methylglucamine (Fig. 3). The mechanism of the excretion of an increasingly more concentrated urine is unclear, but it could be due to a variety of factors, including: (a) an increase in antidiuretic hormone secretion rate;[27] (b) a decrease in loop of Henle activity;[13] (c) decrease in tubular fluid flow to the loop of Henle;[1] or (d) a decrease in rate of removal of sodium by the distal tubule;[23] and (e) a change in medullary blood flow.[2] Since glomerular filtration rate and renal blood flow failed to show any changes, it appears unlikely that hemodynamic effects would account for the decrease in free water clearance. Also, the lack of an increase in osmolar clearance makes it unlikely that a change in nephron activity sufficient to account for this observation is applicable. The most likely explanation is a change in antidiuretic hormone secretion, perhaps induced by the initial osmotic

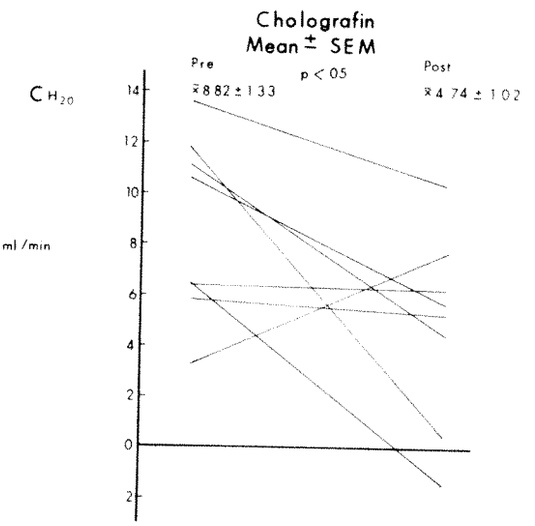


FIG. 3. Clearance of water before and after cholografin injection. (Each line represents 1 person.)

load of iodipamide methylglucamine.[25] The plasma osmolality did not change in these studies, but the observations were made at least 1 hour after the iodipamide methylglucamine was administered and by this time, plasma osmolality alterations could have returned to normal. It is conceivable that the initial increase in plasma osmolality induced by the infusion of iodipamide methylglucamine caused a release of antidiuretic hormone, and by the time the renal function studies were repeated, the patients were in the waning phase of this effect. The net result was the fall in free water clearance.

The changes in renal function after slow infusion of iodipamide methylglucamine were not associated with any discernible deleterious effect. However, the combination of increasing uric acid excretion rate plus increasing urinary concentration would seem to increase the potential for uric acid nephropathy. Consequently, it would be advisable to hydrate the patient prior to intravenous cholangiography. Since the rapidity of injection may have other hemodynamic effects, including an increase in kidney size,[16] changes in plasma volume,[15] and a reduction in renal blood flow,[16] it also appears safer to use a slow infusion technique.

SUMMARY

A study of 10 patients following intravenous infusion of 40 ml. of iodipamide methylglucamine diluted with normal saline to 100 ml., administered in a one half-hour period, resulted in an increase in uric acid clearance and a decrease in free water clearance.

There were no changes in clearance of inulin, paraminohippuric acid, osmoles, urine pH or calculated renal blood flow. Opacification of the biliary ducts was above average in 8 of the 10 patients studied.

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COMBINED PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC) AND SELECTIVE VISCERAL ANGIOGRAPHY (SVA) IN OBSTRUCTIVE JAUNDICE*

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DURING the last 2 decades, percutaneous transhepatic cholangiography (PTC) has proved valuable in the investigation and management of known or suspected obstructive jaundice.[8,11,12] Important information may also be obtained by a more recent method—selective visceral angiography (SVA).[2,4,6,9,10]

The purpose of this report is to evaluate the combined use of these 2 methods in obstructive jaundice.

MATERIAL AND METHOD

The hospital records and the roentgenograms of 50 consecutive combined examinations were reviewed. The patients' ages ranged from 38 to 82 years (mean 62 years). In all but 2 cases the diagnosis (hepatitis and passage of choledochal stone, respectively) had been confirmed at surgery or autopsy. The indications and contraindications of the examinations are given in Table 1.

The roentgen examinations were performed by television fluoroscopy and under local anesthesia. For PTC a nylon catheter with a mandrin was inserted intercostally in the right midaxillary line. Meglumine metrizoate (Isopaque Cerebral, Nyco, Norway) was injected by hand in an amount sufficient to obtain a satisfactory filling of the biliary tree. Films were exposed in 4 to 6 projections. Angiography was performed with red catheters (ÖL 1, thin-walled, 60 cm., 2 side holes) inserted via the femoral artery. Films were exposed in anteroposterior and right oblique projections, stereoscopic films in both projections.

The procedures were carried out by radiologists in the same laboratory. Forty-five patients were subjected to laparotomy, 26 of them on the same day as PTC, and 19 up to 5 months later.

TABLE I

INDICATIONS FOR PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC) AND SELECTIVE VISCERAL ANGIOGRAPHY (SVA)

	No. of Cases
1. Suspected or known extrahepatic biliary stasis of unknown cause	45
2. Earlier operation(s) in the upper right abdomen with suspected or known peroperative biliary duct lesion	14
3. Longstanding jaundice of obscure type	2

CONTRAINDICATIONS TO PTC AND SVA

1. General condition of the patient not allowing laparotomy
2. Hypersensitivity to the contrast medium
3. Thrombotest value below 12 per cent

RESULTS

The findings are summarized in Tables II and III, and some cases are illustrated in Figures 1 through 5. Seventy-two per cent of the patients had tumors. Of these, 86 per cent were diagnosed preoperatively at PTC and 89 per cent at SVA. In only 1 patient was a tumor missed at both examinations. It was a case of recurrent carcinoma of the extrahepatic bile ducts, where earlier operation had distorted the anatomy and where the proper hepatic artery had been ligated.

In 5 patients (PTC failures), only SVA had permitted the correct diagnoses. These

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TABLE II

RESULTS OF PTC AND SVA

Final Diagnosis	No. of Cases	Percutaneous Transhepatic Cholangiography				Selective Visceral Angiography			
		+	−	N	F	+	−	N	F
Free bile duct(s)	2				1			2	
Hepatitis	1				1			1	
Passage of stone(s)	1			1				1	
Choledocholithiasis	4	2			2			4	
Operative lesions	4	4					1	2	1
Strictures, stenoses	3	3					1	2	
Fistulas	1	1							1
Stenoses due to inflammatory changes	4	3			1	4			
Pancreatitis	3	3				3			
In or around bile ducts	1				1	1			
Tumors in or around extrahepatic bile ducts	33	30			3	29	3		1
In extrahepatic bile ducts	11	10			1	9	1		
Pancreatic or periampullary tumors	20	18			2	18	2		1
Metastases	1	1				1			
Anaplastic cancer	1	1				1			
Liver tumors	3	1			2	3			
Total	50	40		1	9	36	4	8	2

+ = stated or suggested diagnosis; − = missed or false diagnosis; N = normal; F = failure.

were: (1) hepatoma; (2) carcinoma of the liver hilus; (3) inflammatory process (abscess) of the liver hilus; (4) periampullary carcinoma with liver metastases; and (5) cystadenoma of the pancreas.

In 9 patients only PTC had yielded the correct diagnoses. These were: (1) carcinoma of the extrahepatic bile ducts (aortography performed); (2) postoperative stenosis of the common hepatic duct (SVA demonstrated tumor of the liver hilus); (3) postoperative fistula of the common hepatic duct (aortography performed); (4 and 5) postoperative stenosis of the common hepatic duct (SVA normal); (6 and 7) choledocholithiasis (SVA normal); and (8 and 9) periampullary carcinoma (SVA normal).

In the case of postoperative fistula, SVA demonstrated ligation of the common hepatic artery, and in 1 case of stenosis, ligation of the right hepatic and gastroduodenal artery.

In 3 instances both examinations failed to reveal the diagnosis: (1) recurrent carcinoma of the extrahepatic bile ducts; and (2 and 3) choledocholithiasis. Here puncture for PTC failed, while SVA of the patient with tumor demonstrated only ligation of the proper hepatic artery (see above).

SVA furnished supplementary information in 24 cases (Table III). There were 8 patients with liver metastases, which were revealed at angiography in 6 (including 1 in whom metastasis had been demonstrated also at PTC). In 19 patients the combined procedure demonstrated that the lesion was

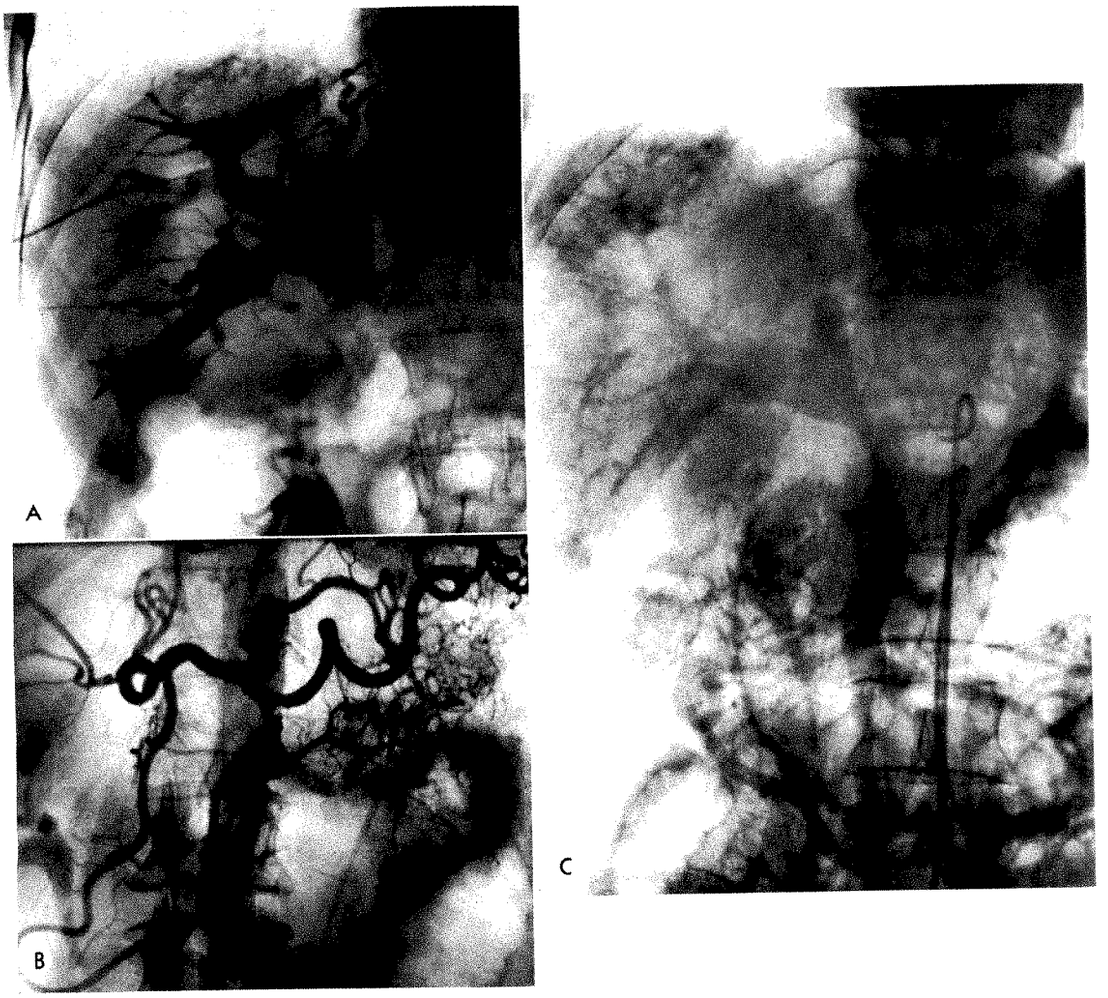


Fig. 1. *Carcinoma of the extrahepatic bile ducts.* (*A*) Total occlusion of the common hepatic duct. (*B*) The tumor extends from the periampullary region to the liver hilus. (*C*) Severe compression of the portal vein.

inoperable. In 5 of them, this had been shown only by SVA (for instance by showing liver metastases or extensive infiltration of the liver parenchyma around the liver hilus). Displacement and/or impression of the portal vein was noted in 6 cases. In 3 of these, the tumor was found to be inoperable, not because of its proximity to the portal trunk, but because of its size and involvement of other structures. In 1 woman the portal vein was markedly displaced and compressed by a cystadenoma of the pancreatic head. Furthermore, in 1 case chronic pancreatitis had compressed the portal vein.

Table III

VALUABLE INFORMATION OBTAINED ONLY BY SVA

	No. of Cases
1. Origin of the pathologic process	5
2. Nature of the pathologic process (cancer, inflammation)	6
3. Extent, engagement of adjacent structures	16
4. Liver metastases	5
5. Anomalous or deranged vessel anatomy	6
	Total 38

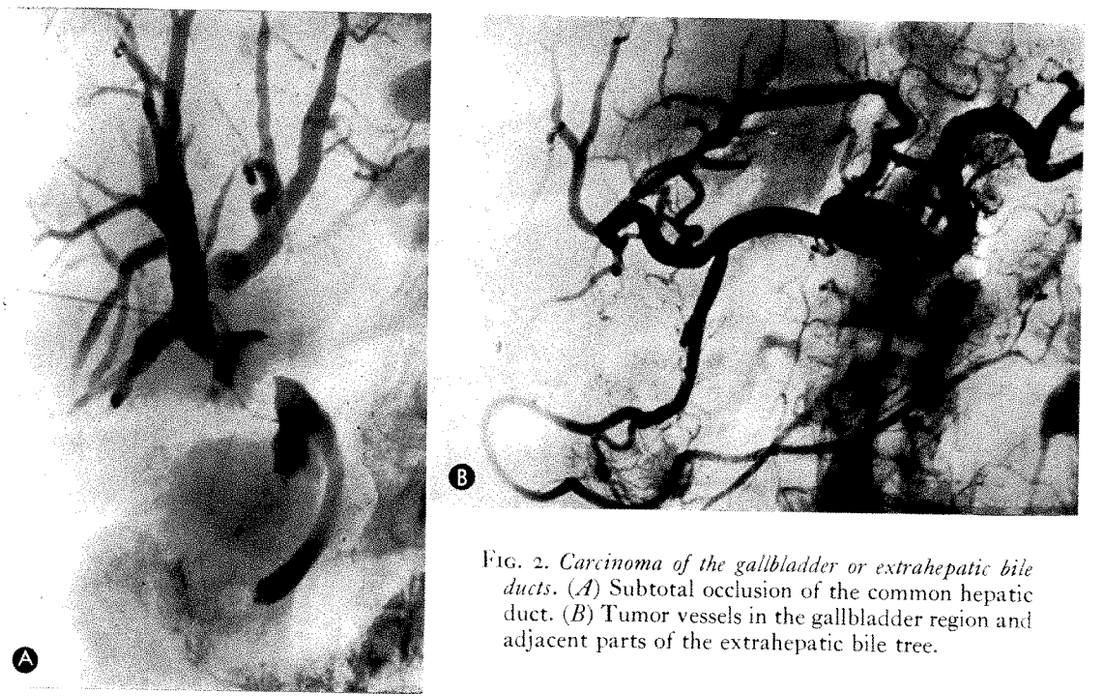


FIG. 2. *Carcinoma of the gallbladder or extrahepatic bile ducts.* (*A*) Subtotal occlusion of the common hepatic duct. (*B*) Tumor vessels in the gallbladder region and adjacent parts of the extrahepatic bile tree.



FIG. 3. (*A* and *B*) *Chronic pancreatitis.* Cholecystectomy performed 20 years earlier.

Transhepatic punctures were successfully performed in 41 out of 50 patients (Table II). The rate of unsuccessful punctures was high, especially in patients with tumors involving extrahepatic bile ducts or with choledocholithiasis. Puncture was unsuccessful in 2 out of 40 (5 per cent) of the patients with dilated bile ducts and in 3 of the 6 with undilated bile ducts. In 4 cases the width of the intrahepatic bile ducts was unknown. The bile ducts were dilated in at least 2 of the 9 cases, where puncture failed. The patients with undilated bile ducts had liver metastases, hepatitis or suspected passage of stone(s). In the group with unknown caliber of the bile ducts, the patients had carcinoma of the liver parenchyma or of the bile ducts and in 1 case cholangitis.

In 2 patients selective catheterization of the visceral arteries was impossible because of atheromatosis, and the examination was limited to aortography. These angiographies are recorded as failures. In neither of these 2 cases did the aortography yield conclusive information about the causal lesion, the one patient having a neoplasm of the biliary tract, the other a bile fistula. In the latter case, however, the aortography had

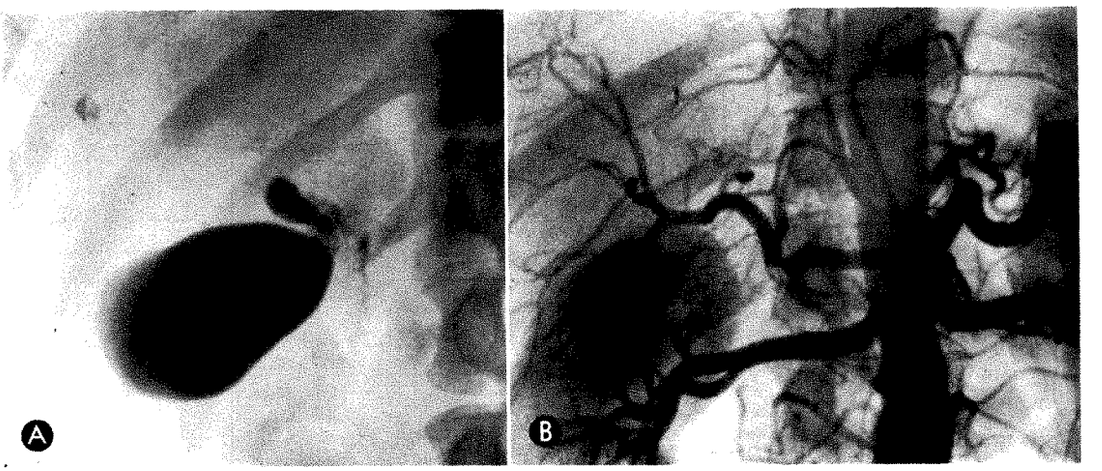


Fig. 4. *Internal bile fistula at the confluence.* A Billroth II operation had been performed 6 weeks earlier. (*A*) Puncture of the gallbladder. (*B*) Subtotal stenosis of the common hepatic artery. No filling of the gastroduodenal artery (aortography performed).

demonstrated ligation of the common hepatic artery.

The PTC was followed by severe leakage of bile (125 ml.) in 1 patient and by severe bleeding (400 ml.) in another. These 2 patients were operated upon a few hours after the PTC. In a further case, PTC was complicated by a liver abscess, successfully drained 2 weeks after the examination. Angiography was never complicated.

In 6 patients SVA was performed a few days after PTC. In 1 of them SVA revealed an arteriovenous fistula, which was, however, no longer demonstrable 11 months later.

DISCUSSION

In 1967 Boijsen and Reuter[3] reported 6 cases of obstructive jaundice, where both PTC and SVA had been performed. They concluded that PTC was suitable for revealing the site of obstruction and the anatomy of the bile ducts, and SVA for demonstrating the origin and extent of the obstruction and hepatic metastases, if any. Both examinations could give information on the cause of the jaundice. This view was corroborated by Bayindir[1] in his report of 14 cases of combined examinations of obstructive jaundice.

In this series, PTC gave no false positive or false negative results. The value of PTC was, however, limited by the frequent (18 per cent) inability of the examiner to puncture the bile ducts. Furthermore, PTC often failed to establish the origin and extent of a tumor and sometimes it could not reveal the nature of the lesion with any degree of certainty. For instance, a firm differential diagnosis between pancreatitis or postoperative stenosis and carcinoma was not often possible. Liver metastases could be demonstrated by PTC in only 1 out of 6 patients. In these respects, SVA furnished extra information. The angiographic examination also showed derangement or anomaly of the vascular anatomy.

Miller *et al.*[7] used combined PTC and splenoportography in 15 patients with biliary pancreatic carcinomas. They concluded that the examinations revealed the possibilities of curable resections. In their series of cases "all degrees of involvement of the portal system associated with pancreaticobiliary carcinoma were noted. In all of the cases where any abnormality of the portal system was seen, from slight external compression to complete obstruction, the tumor was found to be too far advanced for curative resection." In our experience this is not always true. External compression and/or dislocation of the portal vein (as opposed to infiltration and severe obstruction) does not *per se* imply unre-

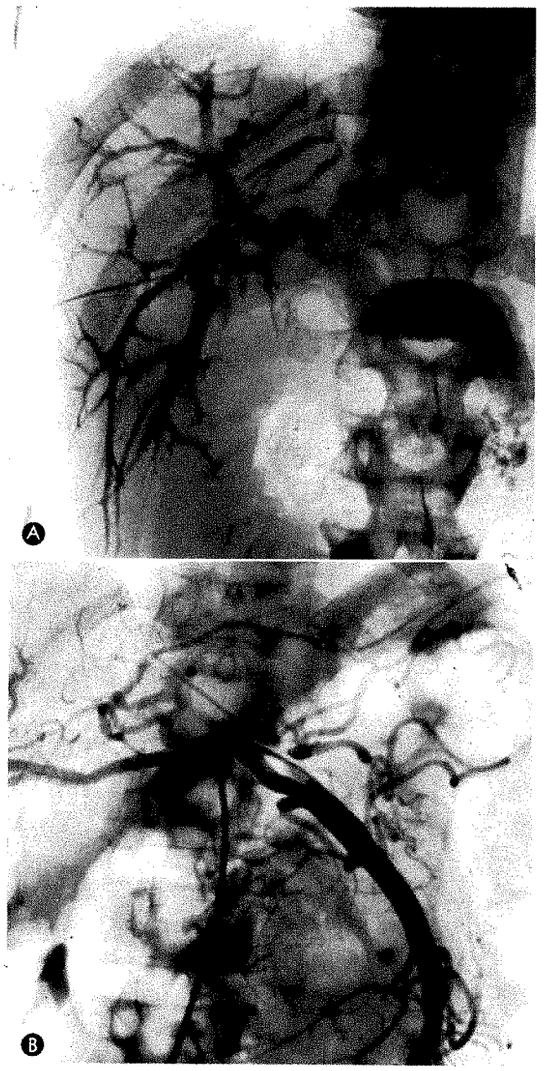


FIG. 5. (*A* and *B*) *Chronic pancreatitis.* Choledochoduodenostomy performed 1 year earlier, cholecystectomy and splenectomy several years earlier. Note the pronounced displacement of the superior mesenteric artery. No signs of tumor or pancreatic pseudocyst.

sectability. Here, it is the extent of the tumor that determines whether radical surgery is possible. Therefore the SVA, which gives detailed information about the nature and extent of the tumor, should be preferred to splenoportography. Naturally, the portal vein should always be examined at SVA.

According to Frommhold,[5] PTC, especially when combined with SVA or splenoportography, should be performed very restrictively as it exposes the patient to certain risks. We do not share his opinion. The information obtained by the combined examination makes the operation easier and less hazardous in these cases, in which the distorted anatomy and the interpretation of pathologic findings are otherwise so often really troublesome to the surgeon. Preoperative knowledge of the anatomy facilitates planning of the operation. Furthermore, it is possible to determine more accurately whether the patient should be operated upon or not. The number of complications in our material was not very high and they were immediately controlled at operation except for the case with a liver abscess.

In the series of Bayindir,[1] and Miller *et al.*[7] the patients had contrast medium in the bile ducts during visceral angiography and splenoportography, respectively. Since the frequently large amounts of contrast medium in the dilated bile ducts may conceal otherwise angiographically demonstrable changes, we prefer to perform the examinations on different days.

SUMMARY

Percutaneous transhepatic cholangiography (PTC) and selective visceral angiography (SVA) were performed in 50 patients with suspected or known obstructive jaundice.

In 3 cases (1 tumor) both examinations failed to reveal the correct diagnosis.

In most of the cases each examination yielded important information, often complementary to that of the other.

Transhepatic cholangiography is suitable for revealing the site of obstruction and the anatomy of the bile ducts. Selective angiography provides information of the origin and extent of the lesion as well as possible hepatic metastases and involve-

ment of nearby structures. Both examinations can give information, often complementary, on the nature of the lesion.

The authors recommend the combined use of PTC and SVA in all patients with known or suspected obstructive jaundice not evidently due to choledocholithiasis, provided that the general condition of the patient allows laparotomy.

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COMPLICATIONS OF PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC)*

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PERCUTANEOUS transhepatic cholangiography (PTC) is valuable in the investigation of suspected or known obstructive jaundice. It is, however, attended by certain risks, especially bile leakage and bleeding.[1,7,11,12]

This paper reports a study of the severity and frequency of complications based on correlation with the diagnosis, laboratory tests, duration of jaundice and width of the bile ducts.

MATERIAL AND METHOD

The material consisted of 79 consecutive patients, 43 males and 36 females, aged 4 months to 82 years (mean 61 years).

The indications and contraindications of PTC are shown in Table I.

TABLE I

INDICATIONS FOR PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC)

	No. of Cases
1. Suspected or known extrahepatic biliary stasis	67
2. Suspected or known bile duct lesion if intravenous cholangiography was not diagnostic	25
3. Longstanding jaundice of obscure type	7
4. Suspected biliary atresia	1

CONTRAINDICATIONS TO PTC

1. Hypersensitivity to the contrast medium
2. General condition not allowing laparotomy
3. Thrombotest value below 12 per cent

The diagnoses (Table II) were verified at laparotomy or autopsy in all but 3 patients. The serum bilirubin (bil./s.) ranged from 1.7 to 48.4 (mean 15.5) mg./100 ml. and the thrombotest (TT) value from 13 to well over 100 (mean 50) per cent (Fig. 1). By the time of the examination, the patients had had jaundice for 1–102 weeks, on the average 9 weeks. In 14 patients the duration of the jaundice was unknown. In 6 patients neither the serum bilirubin level nor the thrombotest value was known at the time of the examination.

The PTC was performed under local anesthesia and television fluoroscopy. In apnea, a nylon catheter (ID/OD 1.0/1.3 mm., length 20 cm.), threaded on a steel cannula, was introduced percutaneously in the midaxillary line in the ninth intercostal space and advanced towards the liver hilus. At most 4 attempts in different directions were made. When puncture was successful, meglumine metrizoate (Isopaque Cerebral, Nyco, Norway) was injected in an amount sufficient to obtain a complete filling of the bile ducts.

The width of the intrahepatic bile ducts was estimated from peroperative cholangiography with Seldinger's criteria,[11] *i.e.*, the width was taken as the mean of the 3 widest ducts in the right lobe (normal 1.5–4 mm.). The examinations were carried out by different radiologists at the same laboratory. Forty-seven patients had laparotomy a few hours after the PTC; in 26 patients operation was performed 1 day to 5 months after the examination; 6 patients were not operated upon.

The complications were classified on the basis of notes in the patients' records. They are listed in Table II, where leakage of bile or loss of blood in amounts too small to be measured is classified as "slight."

The thrombotest determinations were carried out in the way described by the manufacturer (Nyegaard & Co., Oslo, Norway). Values of 50 per cent or more are

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TABLE II

COMPLICATIONS RELATED TO DIAGNOSIS

Final Diagnosis	No. of Patients	Complication							
		Bile Leakage		Bleeding		Liver Abscess	Pain	Other Complication	Total
		Severe	Slight	Severe	Slight				
Free bile ducts	4								
Hepatitis	2								
Passage of stone(s)	2								
Choledocholithiasis	8								
Operative lesions	11								
Strictures, stenoses	8								
Fistulas	3								
Stenoses due to inflammatory changes	5								
Pancreatitis	3								
In or around bile ducts	2								
Tumors in or around extrahepatic bile ducts	47	2	2	2	2	1	1		10
In extrahepatic bile ducts	19	2	1	1	2		1		7
Pancreatic or periampullary tumors	24		1	1		1			3
Metastases	4								
Liver tumors	3								
Biliary atresia	1								
Total	79	2	2	2	2	1	1	0	10

normal. Values above 100 per cent had been recorded as 100.

The findings in Tables III–VI have been evaluated statistically with Wilcoxon's test.

RESULTS

Complications occurred only in patients with tumors (Table II). In 1 case (bil./s. 2.5 mg./100 ml., TT 31 per cent) there was 125 ml. of bile in the abdomen and in another (bil./s. 9.6 mg./100 ml., TT 40 per cent) 400 ml. blood. In a third patient (bil./s. 9.7 mg./100 ml., TT 78 per cent) there was persistent bleeding and bile leakage at the time of operation. All the patients with demonstrable bile leakage or bleeding were operated upon within a few hours of PTC.

A liver abscess appeared in a woman with a cystadenoma in the head of the pancreas. The abscess was drained of 600 ml. of pus 2 weeks after PTC and the patient recovered completely. One patient had severe pain in the right hypochondrium for 24 hours. The cause of this pain could not be explained despite operation.

The frequency of complications was not significantly ($p > 0.05$) correlated with the duration of the jaundice, the level of bilirubinemia or the TT value (Tables III–VI; Fig. 1).

Dilated bile ducts could not be punctured in 5 out of 65 patients (Table VII). The corresponding figures for normal bile ducts were 5 out of 8.

TABLE III

COMPLICATIONS RELATED TO THE DURATION OF JAUNDICE IN WEEKS

	No. of Patients	Mean Value	Range
Complications	7	4·4	1–9
No complications	58	9·4	1–102

TABLE IV

COMPLICATIONS RELATED TO THE DEPTH OF JAUNDICE

	No. of Patients	Mean Value	Range
Complications	9	11.0	2.5–20.2
No complications	64	16.1	1.7–48.4

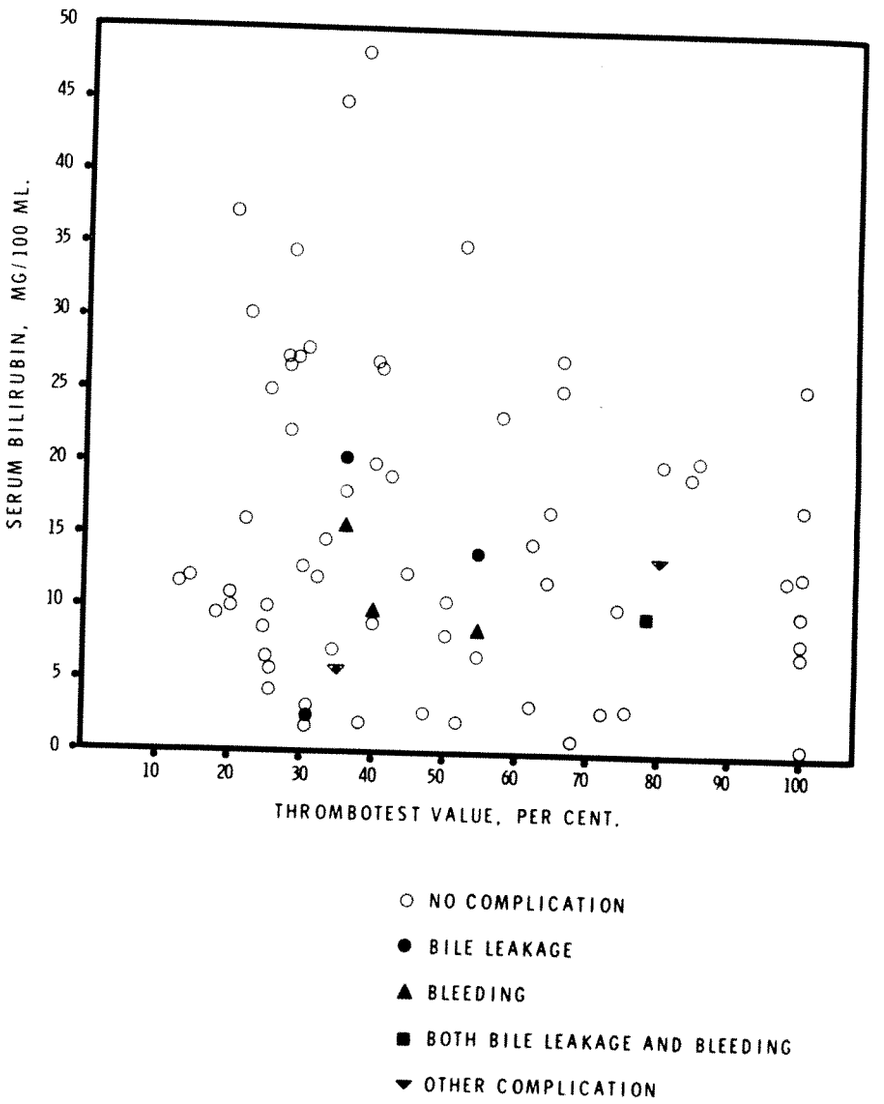


FIG. 1. Serum bilirubin and thrombotest values related to complications of percutaneous transhepatic cholangiography (PTC).

TABLE V

COMPLICATIONS RELATED TO THE THROMBOTEST VALUE IN PER CENT

	No. of Patients	Mean Value	Range
Complications	9	50	31–78
No complications	64	51	13–100

TABLE VI

BLEEDING RELATED TO THE THROMBOTEST VALUE IN PER CENT

	No. of Patients	Mean Value	Range
Bleeding	4	53	38–78
No bleeding	69	49	13–100

All but 1 complication occurred in patients with dilated bile ducts. In 1 patient with extensive extrahepatic bile duct carcinoma and biliary stasis, the examination was followed by slight bleeding, but as peroperative cholangiography had not been done, the width of the ducts is recorded as unknown.

Complications were more common when the attempts failed (25 per cent) than when they were successful (10 per cent). Of those cases in which the bile ducts were dilated and puncture unsuccessful, complications occurred in 60 per cent. Puncture had never been followed by complications in patients with bile ducts of normal caliber. Puncture of the gallbladder in 2 patients produced no complications.

In 6 patients angiography of the celiac axis a few days after the PTC revealed a small arteriovenous fistula in 1. It was no longer demonstrable at control angiography 11 months later.

The frequency of complications did not vary with the age of the patients.

In no case had the complications resulted in shock or death.

DISCUSSION

The over-all frequency of complications of PTC is about 5 per cent in published series. Biliary peritonitis is reported to occur in an over-all frequency of 3 per cent.[12] This figure probably refers to cases not operated upon immediately after the examination. Bile leakage without clinical

TABLE VII

COMPLICATIONS RELATED TO THE WIDTH OF THE INTRAHEPATIC BILE DUCTS

Width	Puncture	Bile Leakage		Bleeding		Liver Abscess	Pain	Other Complication	Total
		Severe	Slight	Severe	Slight				
Increased (65)	Success (60)	1	2	1	1		1		6
	Failure (5)	1		1		1			3
Normal (8)	Success (3)								
	Failure (5)								
Unknown (6)	Success								
	Failure (6)				1				1
Total (79)	Success (63)	1	2	1	1		1		6
	Failure (16)	1		1	1	1			4
Total (79)		2	2	2	2	1	1	0	10

peritonitis has been noted in an additional 1.7 per cent.[12] Intraabdominal hemorrhage has occasionally been reported and then mainly among patients in whom preoperative examination had revealed abnormal coagulation. It is difficult to compare the frequency and severity of complications in published series because of differences in technique and range of indications. Moreover, most authors do not state how often or when laparotomy had been performed. The present investigation is based on hospital records. Only 47 out of 79 were operated upon on the day of the examination. The frequency of minor complications (above all minor bile leakage and bleeding) not producing noteworthy symptoms was probably higher than that reported here.

According to some authors, *e.g.*, Flemma *et al.*,[3] and Hunter,[5] a normal clotting mechanism is a prerequisite for the examination. Others state that the procedure should not be carried out if the Quick value is below 60–70 per cent[1,2] or if the prothrombin time is prolonged 4 or more seconds over the control.[7] The above-mentioned values correspond roughly to TT values of 20–30 per cent and 30–40 per cent, respectively. However, judging from our findings, there is no relation between the frequency and severity of complications and the TT value, provided it is above 12 per cent.

The complications in our series occurred only in patients with tumors obstructing the bile ducts. We cannot explain this. It might, however, be mentioned that Hedner and Nilsson[4] have demonstrated abnormal amounts of fibrinogen degradation products (FDP) in the serum of 61 per cent of all cancer patients. It is thought that FDPs act essentially by inhibiting the polymerization of fibrin monomers.[8] Furthermore, several workers, *e.g.*, Peterson,[10] have shown that certain tumors contain fibrinolytic substances. The concentrations of FDP occurring in disease do not influence the results of the above-mentioned tests.[4,8] Although various diseases of the liver are known to be associated with an increased bleeding tendency, we did not find any clear correlation between the results of the tests and the risk of bleeding (or other complications). The thrombin time may perhaps give a more reliable estimation of the risk of bleeding in these cases.[8]

The increased frequency of complications in patients with dilated bile ducts may be explained by an increased bile pressure, which keeps the puncture track open with escape of bile and blood as a result. We, therefore, recommend drainage of the bile and contrast medium before the withdrawal of the catheter. This procedure has recently been described by Ozdemir and Lancaster,[9] who used it in 17 patients without any complications.

SUMMARY

Percutaneous transhepatic cholangiography (PTC) was carried out in 79 patients with known or suspected obstructive jaundice.

Complications were noted in 10 patients with tumors (bile leakage 4, bleeding 4, pain 1, liver abscess 1), and in at least 9 of them the bile ducts were dilated.

All patients with bile leakage or bleeding were operated upon within a few hours of the examination, thus minimizing the risk of complication.

No correlation was found between the complications and the thrombotest value (provided it was above 12 per cent) or the depth and duration of the jaundice.

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DETECTION OF MALIGNANT DISEASE BY PERORAL RETROGRADE PANCREATICO-BILIARY DUCTOGRAPHY*

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CANNULATION of the ampulla of Vater through the fiberoptic duodenoscope is now performed in many centers.[1,3,4,6,7,10] Retrograde ductograms of the biliary tree and pancreas are obtainable with a high degree of reliability and safety.[1,4,7]

The present report is an assessment of this procedure in the evaluation of patients with suspected neoplastic disease of the liver and pancreas.

MATERIAL AND METHOD

Between November 1971 and July 1972, 52 patients with pancreatic or biliary tract disease were studied and ductography was attempted. Of these, 28 patients were suspected cases of neoplasm of either the liver or pancreas. The method used has been described in detail in previous publications.[6,7]

In brief summary, the procedure entails passing a teflon cannula (1.7 mm. O.D.) through the Olympus JFB duodenoscope into the ampulla of Vater. Contrast material, sodium meglumine diatrizoate, is then injected into the cannulated duct system. When only the pancreatic duct is filled, approximately 2–3 cc. is required. When the biliary tree is successfully cannulated, up to 15 cc. is used. The patients were medicated with 10–20 mg. diazepam intravenously (Valium),* 0.5 mg. atropine intramuscular and 60 mg. dicyclomine hydrochloride intramuscular (Bentyl).† Instillation of an antifoaming agent, dimethyl silicone, into the duodenum is frequently required. In the more recent cases, 5–10 mg. propantheline bromide intravenously (Pro-Banthine)‡ has been the only anticholinergic used with great success.

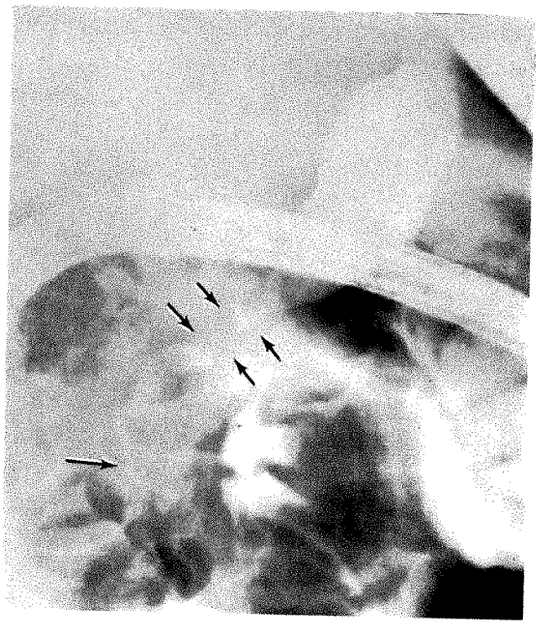


FIG. 1. A 75 year old male entered with a very brief history of jaundice and itching. Except for icterus, the physical examination was negative. The laboratory data were consistent with obstructive jaundice.

Biliary ductogram shows an annular constricting lesion of the common bile duct (double arrows). The large metallic curvilinear object is the endoscope. The small catheter (single arrow) projects from it into the common duct.

A carcinoma was confirmed at surgery and a bypass procedure performed.

RESULTS

Of the 28 patients evaluated for sus-

* Roche.

† Merrell-National.

‡ Searle & Co.

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pected malignancy, visualization of either pancreatic or biliary ducts was obtained in 19 individuals. This compares favorably with results obtained by others.[1,4,6,7] Success in cannulating the duct of choice was not always obtained. Of 18 cases where the biliary tree was considered the primary objective, 10 were successfully cannulated. Of the 9 cases where the pancreatic ducts were considered to be the primary target, 7 ductograms were obtained. It is apparent that in many cases definition of the "duct of choice" is at best arbitrary, as in many instances knowledge of either is a valuable contribution. Thus, in 9 patients, the non-primary target duct was opacified and provided valuable information. It should be stressed that in many instances the study was concluded after the duct of choice was cannulated rather than prolong the procedure unnecessarily.



Fig. 2. A 51 year old male with a 2 week history of jaundice. The patient had intermittent right upper quadrant abdominal pain for 3 months. He had undergone cholecystectomy in the past. Except for icterus, the physical examination was normal. The laboratory data were consistent with obstructive jaundice.

Cannulation of the biliary tree was successfully performed which demonstrated no evidence of obstruction. The final diagnosis was cholangitis.

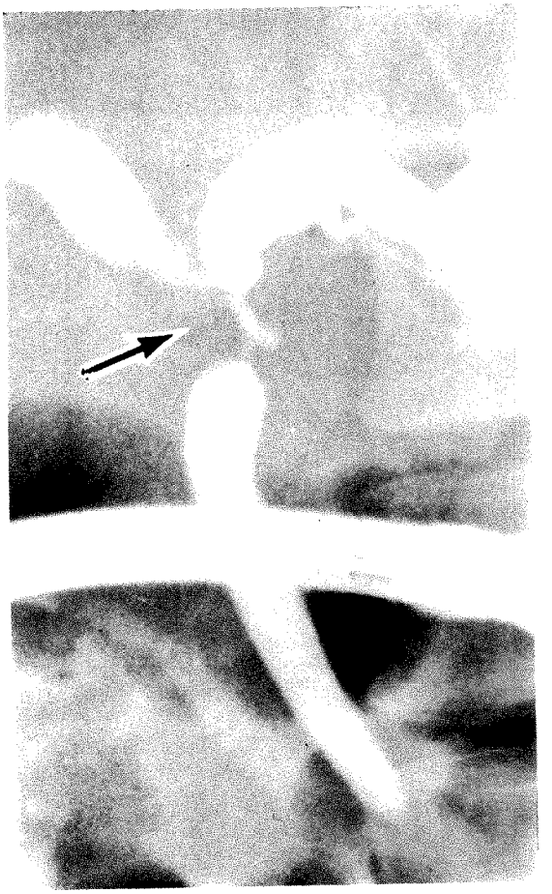


Fig. 3. A 48 year old alcoholic entered with a 1 month history of increasing abdominal pain and jaundice. The liver was noted to be enlarged. The laboratory data included significantly elevated bilirubin, alkaline phosphatase and cholesterol levels. Gastrointestinal series was unremarkable.

The common bile duct was successfully cannulated, demonstrating an obstructing lesion at the origin of the common hepatic duct (arrow). The final diagnosis was metastatic carcinoma, primary unknown.

Of the 28 cancer suspects, 8 were subsequently proven to have neoplastic disease at operation. Four were diagnosable on the ductograms obtained. Three of these cases

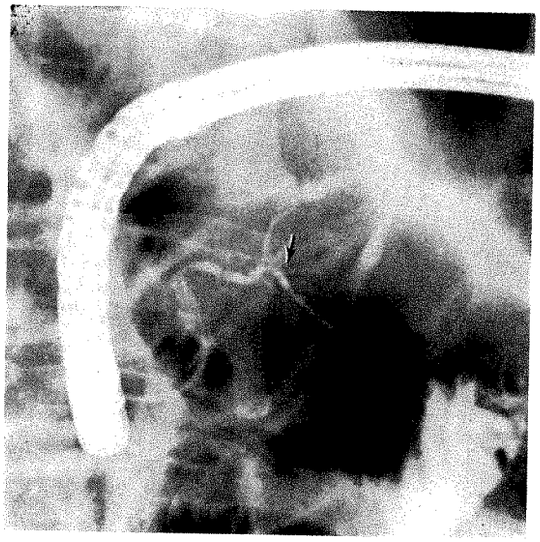


FIG. 4. A 64 year old man entered the hospital for evaluation of progressive anorexia, weight loss and occasional diarrhea of 5 months' duration. He had noted jaundice for 1 month. There was no pain. The only remarkable physical finding was the presence of jaundice. The bilirubin was moderately elevated and the other blood chemistries were normal. The gastrointestinal series was unremarkable.

Cannulation pancreatic ductogram shows obstruction of the main pancreatic duct 2.5 cm. from the orifice (arrow). The common bile duct is not opacified.

Tissue diagnosis was pancreatic carcinoma.

are shown in Figures 1, 3, and 4. Despite failure of the cannulation procedure in 4 patients, an endoscopic diagnosis of periampullary carcinoma was made in 3 and a large extrinsic mass compressing the stomach noted in the fourth. Thus, of 8 surgically proven cases, all were recognized preoperatively either by ductography or endoscopy.

Of the 19 patients who were jaundiced, 4 were shown to have normal bile ducts—a demonstration that obviated surgical exploration (Fig. 2). Four patients were shown to have benign pathology: choledochocholelithiasis, cholecystocholelithiasis, or changes of pancreatitis (Fig. 6, *A* and *B*). Two were shown to have findings of neoplasm in the biliary tree (Fig. 1, and 3). Of the 8 patients in whom biliary ductography failed, 3 were found to have neoplasm endoscopically and 1 had an abnormal pancreatic ductogram due to pancreatic carcinoma (Fig. 4). Thus, in only 4 jaundiced patients was the study not significantly contributory.

Of the 9 cases where the pancreatic duct was the principal target, no ductogram whatsoever was obtained in 2. One ductogram showed an obstructing lesion of the main pancreatic duct (Fig. 4), subsequently proven to be malignant. In 5 patients, the ductograms showed a variety of changes: narrowing, displacement, cyst formation (Fig. 6, *A* and *B*), and apparent normality (Fig. 5, *A–C*). All were subsequently proven to have pancreatitis. It appears that the manifestations of this disease are most variable. To assess the diagnostic significance of these findings, a larger series would have to be evaluated.

Complications to date have generally been minor, supporting the experience of other investigators. Occasional transient temperature elevations have been noted. In none of these, however, was there evidence of clinical pancreatitis. Only in 1 patient was the serious problem of ascending cholangitis encountered. This was a patient who had total obstruction of the common duct by carcinoma.

DISCUSSION

Our success rate with the cannulation procedure in patients with suspected neoplasm compares well with previously published data.[1,4,6,7] The procedure can be performed where chemistries obviate the use of oral or intravenous cholangiography.[11] In addition, distention is not a factor in successful visualization of the biliary tree, whereas with the transhepatic approach a normal biliary tree often obviates success.[5] The potential of bile peritonitis encountered with the transhepatic study is not a consideration. The "mini-laparotomy" procedure with intraoperative bile duct needling and opacification advocated by some,[9] requires surgical incision, an operating room, and sterile technique. The endoscopic study requires none of these.

Relatively simple visualization of the pancreatic duct opens an entirely new vista to the diagnostic radiologist. Previously,

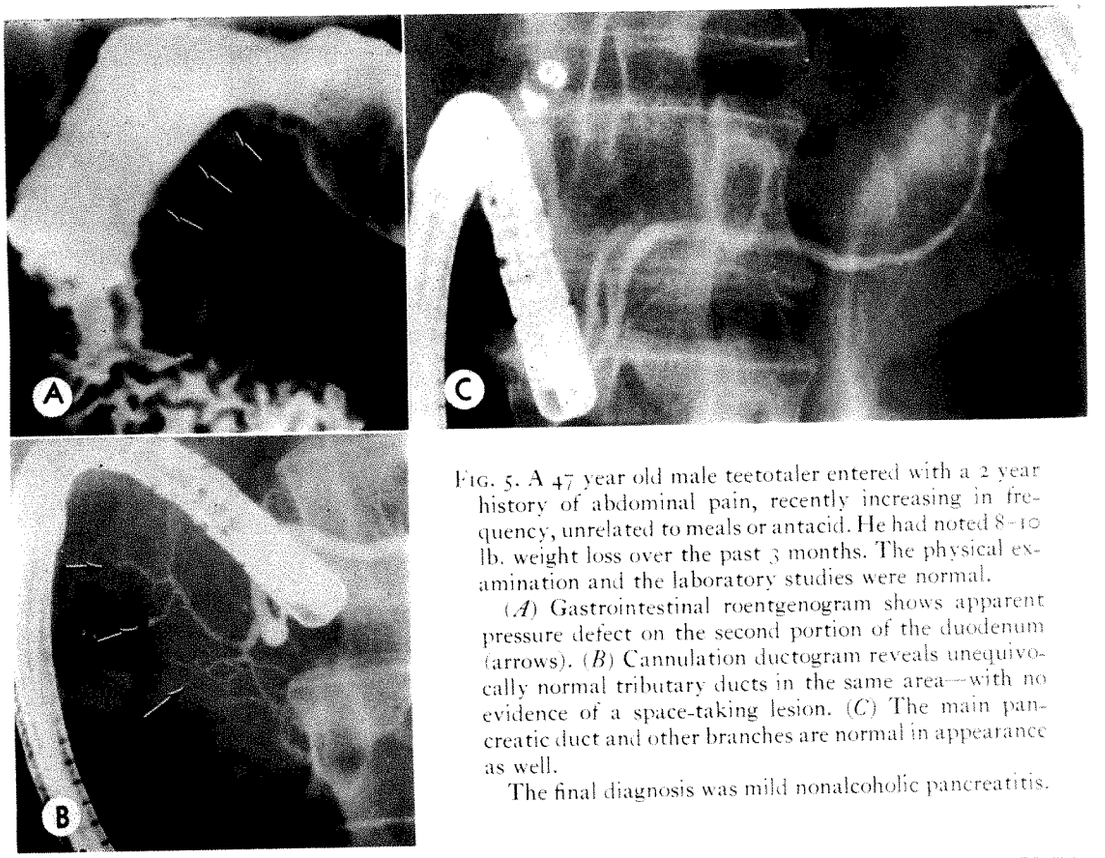


Fig. 5. A 47 year old male teetotaler entered with a 2 year history of abdominal pain, recently increasing in frequency, unrelated to meals or antacid. He had noted 8–10 lb. weight loss over the past 3 months. The physical examination and the laboratory studies were normal.

(*A*) Gastrointestinal roentgenogram shows apparent pressure defect on the second portion of the duodenum (arrows). (*B*) Cannulation ductogram reveals unequivocally normal tributary ducts in the same area—with no evidence of a space-taking lesion. (*C*) The main pancreatic duct and other branches are normal in appearance as well.

The final diagnosis was mild nonalcoholic pancreatitis.

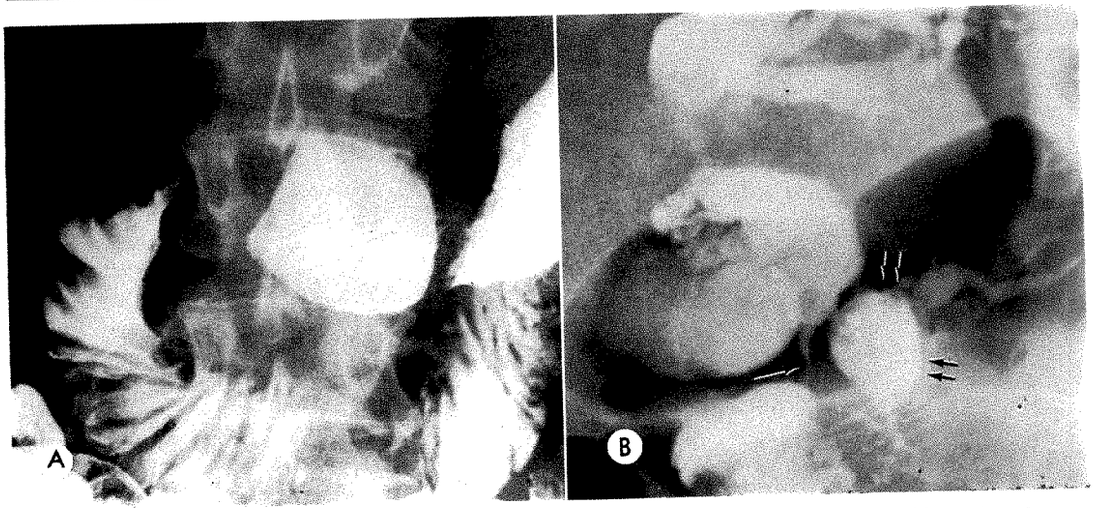


Fig. 6. A 39 year old chronic alcoholic entered with persistent recurrent abdominal pain. He had undergone surgical drainage of a pancreatic pseudocyst 18 months prior to admission. The physical examination revealed icterus and hepatomegaly. The laboratory data included significantly elevated bilirubin and alkaline phosphatase.

(*A*) Gastrointestinal roentgenogram shows evidence of a mass in the head of the pancreas. (*B*) Cannulation of the biliary and pancreatic ducts demonstrates distention of the biliary tree secondary to narrowing of the distal common duct (arrow) by a pancreatic pseudocyst (double arrows). The pseudocyst is noted to contain stones. The proximal pancreatic ducts are dilated and irregular.

The patient was surgically decompressed with prompt relief. No evidence of tumor was noted.

ductograms of the pancreas were obtainable with reasonable success only during laparotomy.[2,8] Knowledge of this usually obscure area is of enormous help to the operating surgeon.

SUMMARY

An assessment of the use of peroral retrograde ductography of the pancreas and biliary tree in the evaluation of suspected neoplasm is presented. Valuable diagnostic and preoperative information is obtainable in a high percentage of cases.

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ENDOSCOPIC PANCREATO-CHOLANGIOGRAPHY*

A PRELIMINARY REPORT ON TECHNIQUE AND DIAGNOSTIC SIGNIFICANCE

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THE recent advances in fiber optics and the increasing availability of flexible endoscopes have made possible direct vision of almost any part of the gastrointestinal tract. With the aid of an x-ray television, fiberduodenoscopy and pancreatography or pancreato-cholangiography may soon be a routine procedure in a large gastrointestinal service of a hospital in this country. Nevertheless, such enthusiasm seems somewhat premature, and a more careful scrutiny is needed before one can decide on the diagnostic value and indication of the procedure, which is not entirely without risk.

Nonsurgical visualization of the pancreatic duct had long been a dream of gastroenterologists. In 1965, Rabinov and Simon[8] succeeded in cannulating the pancreatic duct in 1 patient out of 8, using a specially designed duodenal tube. Three years later, McCune and his associates[5] first reported on endoscopic cannulation and roentgenologic visualization of the pancreatic duct. Their success was quickly emulated by a number of endoscopists in Japan,[3,4,7,9] where endoscopes of high quality have recently been developed, and in Germany[2] as well.

Our experience in duodenoscopic pancreatography may be worth describing, to help assess the clinical value of the procedure in the diagnosis of pancreatic and biliary tract diseases. For the purpose of cholangiography, the percutaneous transhepatic method has already established its place in this country,[6] and the duodenoscopic approach provides another addition to the choice of the technique.

MATERIAL AND METHOD

INSTRUMENTATION

Fiberduodenoscope Model JF-B of Olympus Co., Tokyo, has been used. This instrument is 10 mm. in diameter in its main portion, and has an effective length of 1,250 mm. from the tip to the connection of the flexible portion with the manipulating part. The tip is equipped with a rigid lens system 17 mm. in length, which can be bent at will 120° up and down, and 90° right and left. It contains on one side 2 lenses and 2 holes: one lens is for illumination through an inbuilt light guide system, the other has a fixed focus for observation with depth of a visual field of 5–60 mm. and a visual angle of 64°; the small hole is for injecting air and washing fluid, and the larger hole is for passing a forceps and a cannula, the angle of whose extrusion can be regulated up to 85° by raising its supporting base. The instrument is attached with a connector to a xenon lamp, and for photography to an Olympus Pen-F camera.

PROCEDURE

The patient is given a mild cathartic on the previous night together with 1 gm. streptomycin *per os*, and duodenoscopy is carried out in the morning. The breakfast is withheld; 1 gm. streptomycin and 6 tablets of antifoam Gascon (dimethyl polysiloxane) are given; and 30 minutes before the procedure, 50 mg. demerol and 0.5 mg. atropine sulfate are injected. The patient is placed on the table on his left side, and under x-ray television fluoroscopy, the

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FIG. 1. Normal pancreatogram showing the main duct, the major branches and the accessory pancreatic duct (arrowhead). The cannula was inserted without resistance as far as the midpoint of the main duct—a rare situation. Very little contrast medium filled the branches along the first half of the duct because of the presence of the cannula. The Santorini duct seems to open in the duodenum about 2.5 cm. above the orifice of the main duct.

duodenoscope is inserted into the stomach and then into the duodenal bulb past the pylorus. At this point, the apical part of the instrument is bent and it is slowly forwarded further down the second portion of the duodenum, with the aid of the operator's hands from the outside—the part of the procedure that requires skill and experience. For the observation of the descending portion, air is injected to inflate it. To cannulate the Vater papilla, one has to maneuver the scope in such a way that the papilla is immediately in front of the lens. The papilla is usually readily recognized, but one may have to wait for a few minutes to determine the orifice from which bile flows. Intravenous injection of Secretin facilitates the recognition of the orifice, but it is to be avoided as much as possible for fear of increasing pressure in the pancreatic duct. When the lens is clouded by the duodenal fluid, it is washed out by injecting saline and the antifoam.

The cannulation tube is plastic, 2 mm. in outer diameter with a stylet, and has previously been sterilized with a surfactant detergent and alcohol. Shortly before insertion, the stylet is withdrawn, the cannula is attached to a 20 ml. syringe and a small amount of 60 per cent urografin (Na and meglumine diatrizoate) is injected to expel the air in the cannula. Normally, the cannula is inserted 5–30 mm., sometimes as far as 80 mm. without much resistance (Fig. 1), and then the contrast medium is injected with a minimum manual pressure under fluoroscopy. No force should be exerted in insertion, because of the risk of injuring the duct which can cause seepage of bile or perforation. If air is introduced, it results in abrupt cessation of the flow of the contrast medium, that can be confused with the presence of carcinoma. There is little difference in the result between several water-soluble contrast media which are superior to barium or oily agents.[10]

For a normal pancreatic duct, a few milliliters of the opaque medium suffice to visualize the entire length of the main pancreatic duct, and for its major branches a few more milliliters are needed. The injection is terminated; left lateral and posteroanterior, and sometimes left oblique roentgenograms are taken; then the cannula and the scope are withdrawn; and several more roentgenograms in various projections, including the right oblique view and those in the erect position, are taken in quick succession. The speed of disappearance or excretion of the contrast medium into the duodenum is checked on the television. If carried out properly, the entire main pancreatic duct is visualized with its major branches (Fig. 2; and 3). If injection is continued further and more than 7–8 ml. is used in a normal pancreas, the opaque medium enters the finer branches and the pancreatic tissue (Fig. 4), resulting in a greater rise in serum amylase and always a definite pain. Immediately after the procedure, 100,000 units of Trasylol is injected followed by 1 to 3 more doses at 12 hour intervals, and the administration of 1 to 2 doses of streptomycin for the prevention of acute pancreatitis and infection.

Because of the variability in the anatomic relationship between the terminal Wirsung duct and the common duct, the

result of the pancreatography is not predictable. Generally speaking, if the cannula was inserted more or less straight at a right angle, the chances of obtaining pancreatography are greater, and the choledochus is often visualized when the cannula is inserted obliquely upward. After successful pancreatography, the common duct may be visualized with the cannula withdrawn halfway and the contrast medium re-injected. The accessory pancreatic duct is often visualized due to connection with the Wirsung duct. Although difficult, cannulation of the minor papilla can also be attempted.

CLINICAL STUDY

Barium swallow study and hypotonic duodenography were carried out in all subjects prior to duodenoscopy.

We have done duodenoscopy on more than 80 subjects with only 1 failure, in whom passing the scope beyond the first portion of the duodenum took too long for the patient to tolerate. The Vater papilla was recognized in all but 3. Its shape varied from subject to subject, bearing little relation to the ease or difficulty in cannulation. The 3 cases in which the papilla was not discernible included a pancreatic tumor, stricture due to annular pancreas and cirrhosis with a dilated duodenal loop.

The cannulation failed in 8 out of 55 attempts with the over-all success rate of 85.5 per cent, and pancreatography was made in 39 out of 47, in which both the

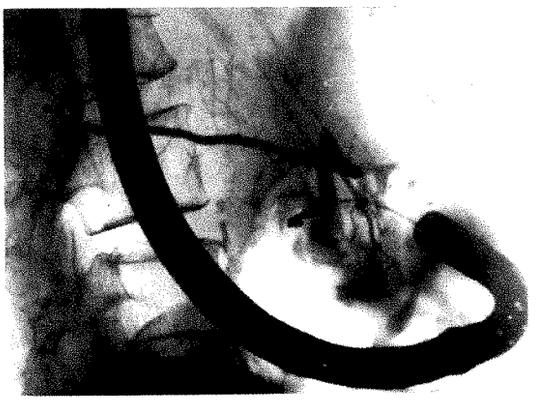


Fig. 3. Lateral pancreatogram, while the cannula is still in place, shows the directional relationship of the head portion of the duct with respect to the body and tail of the pancreas, which courses from the front toward the left and posteriorly. The first branches form almost right angles with the main duct in the body of the pancreas.



Fig. 2. Normal pancreatogram. The course of the main duct across the vertebral column in the posteroanterior projection is more or less typical. The accessory duct branches off the main duct at a point about one-quarter from the duodenal orifice. A small pool of the opaque medium near the papilla was caused by retrograde flow of the medium into the terminal choledochus. The width of the main duct gradually tapers off from the point of the change of direction, somewhere near the junction of the head and the body of the pancreas.



Fig. 4. Simultaneous visualization of the pancreatic duct and the biliary tree including the gallbladder. Because of the slightly excessive contrast medium injected into the pancreatic duct, it entered the finer branches, and penetrated further into the acinar structure (arrowhead).

Table I

CLINICAL MATERIAL AND RATE OF SUCCESS IN PANCREATO-CHOLANGIOGRAPHY

Condition	No. of Subjects	No. of Success in			No. of Failures
		Pancreatography	Choledochography	P.+C.	
Normal	16	13	1	1	1
Chronic pancreatitis	8	6	2		
Pancreatolithiasis	6	2		2	2
Carcinoma of pancreas	4	1		1	2
Cholelithiasis	14	6	2	3	3
Cholangitis	1		1		
Carcinoma of bile duct	1		1		
Insufficiency of sphincter of Oddi	2	1	1		
Hepatoma	1	1			
Metastatic liver carcinoma	1			1	
Hyperthyroidism	1	1			
Total	55	31	8	8	8

pancreatic and common ducts were visualized in 8. In 8 only the common duct was visualized (Table I). The subjects in whom cannulation was carried out consisted of: 20 with normal pancreas as assessed by various tests including selenomethionine scan, Pancreozymin-Secretin test and enzyme studies; 12 cases of chronic pancreatitis including 4 with stones; 2 cases of pancreas carcinoma; 11 cases of cholelithiasis; 1 case of cholangitis; 1 case of metastatic liver carcinoma; 1 case of bile duct carcinoma; and 2 cases of insufficiency of the sphincter of Oddi. No cannulation was attempted in patients with carcinoma of the papilla, but duodenoscopic biopsy was carried out instead.

Although the patients felt some distress or pain upon injection of the contrast medium, analgesics were seldom required. The time during which the contrast medium remained in the pancreatic duct, or the time required for the clearance of the medium after the withdrawal of the cannula, was measured in each subject. It was 4 minutes and 6 seconds on average in the control, and 26.5 minutes in chronic pancreatitis. The posteroanterior roentgenograms were analyzed for the length of the main pancreatic duct, and for its diameter in each of the 3 portions: the head, the body, and the tail. The length of the normal pancreatic duct measured 15.8 mm. on average, and it was slightly longer in chronic pancreatitis. The maximum duct diameter of the head of the normal pancreas was 3.9 mm., and it was 8.3 mm., or more than twice as large in chronic pancreatitis (Table II). The increase in caliber, and hence increased volume of the duct, is reflected in the delayed clearance of the contrast medium. The medium remains in the bile duct longer

Table II

LENGTH AND DIAMETER OF THE PANCREATIC DUCT AND SPEED OF CLEARANCE OF THE CONTRAST MEDIUM

Group	No. of Subjects	Length (cm.)	Diameter (mm.)			Time for Clearance of Contrast Medium
			Head	Body	Tail	
Normal	20	15.7	3.9	3.4	2.1	4 min. 6 sec.
Chronic pancreatitis	10	16.5	8.3	8.7	4.0	26 min. 30 sec.

than in the pancreatic and the common duct.

REPORT OF CASES

Case I. S.M., 58 year old male, was admitted on March 9, 1971, because of loss of weight and postprandial epigastric pains of 2 months' duration. Physical examination revealed a slight rigidity above the umbilicus. Urine gave a (+++) test for sugar and increase in amylase (344 Caraway units/hr.). Blood chemistry was negative except for hyperglycemia and a diabetic type of tolerance curve following 50 gm. of oral glucose. The Pancreozymin-Secretin test showed a marked reduction in pCO_2 and a normal amylase output. A tentative diagnosis of chronic pancreatitis was made.

Pancreatography revealed a rather straight main duct which was abruptly narrowed and obliterated short of the tail of the pancreas (Fig. 5).

A suspicion of malignancy was entertained and an operation was performed to find carcinoma in the tail of the pancreas.

Case II. K.I., 59 year old male, started drinking heavily at the age of 17 years, and had a long history of diabetes mellitus. Because of his negligence, the control had been poor and he developed pulmonary tuberculosis 10 years previously. He had been hospitalized twice for periods of more than 1 year. He had had 2 episodes of jaundice which lasted for 1 and 2 weeks, unaccompanied by a pain. He was admitted to our hospital on January 6, 1970, because of epigastric distress and general malaise, in spite of insulin therapy instituted recently by a physician. Plain roentgenograms of the abdomen taken on admission disclosed small scattered calcified spots in the area compatible with the location of the pancreas.



Fig. 5. Case I. The main duct in the head of the pancreas is somewhat dilated and the contrast medium was blocked immediately after the irregular narrowings in the tail, rendering the length of the main duct rather short. Such termination of the duct should be differentiated from that caused by introduction of an air bubble in front of the opaque medium column. Carcinoma of the pancreas originating in the tail of the pancreas was found at operation.

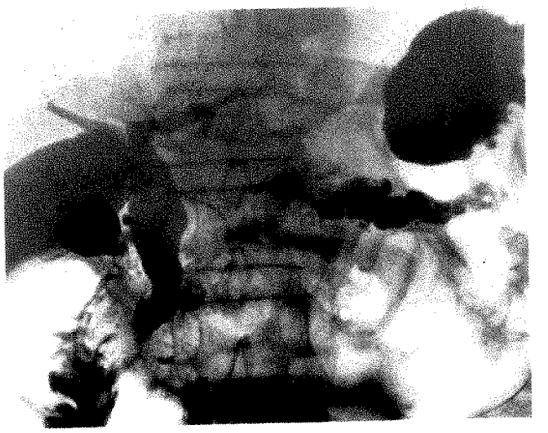


Fig. 6. Case II. Both the pancreatic duct and the choledochus are markedly dilated. Many small calculi along the main pancreatic duct are seen, and they are superimposed on the contrast medium. Superimposed opacities are also discernible in the tail of the pancreas. The dilated ducts are tortuous and irregular. Because of the lapse of time, the opaque medium has already flowed out of the head and the body of the pancreas, rendering visualization of small calculi in its wake. The wall of the lower choledochus is rigid, suggesting a sclerosing process in the head of the pancreas that surrounds it.

Pancreato-cholangiograms showed markedly enlarged pancreatic and common ducts, and small calculi superimposed on the contrast medium in the former (Fig. 6).

Case III. S.K., 68 year old male, was admitted on July 12, 1971, because of right-sided lumbago. He started having pain in the right lumbar region about 1 year previously, and occasionally in the right flank. He had a gastric ulcer about 10 years ago, and was told of abdominal calcifications 2 years ago when he had an upper gastrointestinal series. On admission, there was a mild anemia, but blood chemistry was within normal limits. Roentgenologic

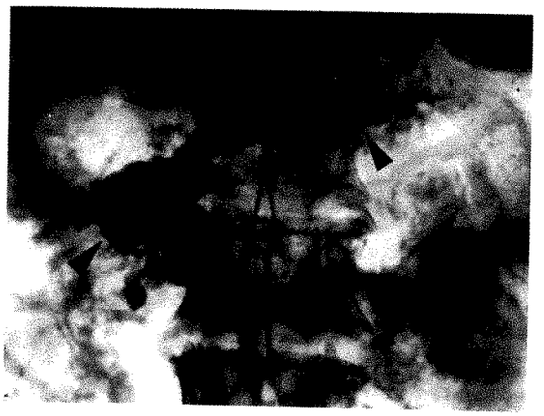


FIG. 7. Case III. Chronic pancreatitis with stones. The markedly dilated and tortuous duct of the pancreas is apparent. The 2 large stones are in the duct, casting a round and an oval density (arrowheads) enhanced by summation of the stone and medium opacities. Other smaller stones seem to be in the duct producing irregular dark spots.

studies revealed pancreas stones: a 10×12 mm. stone in the head and an 8×8 mm. stone in the tail, with many small calcifications scattered in their vicinity.

Pancreatography disclosed a markedly dilated and tortuous pancreatic duct and stones superimposed on, or buried in, the contrast medium (Fig. 7).

CASE IV. T.K., 63 year old male, entered the hospital on February 8, 1971, because of severe epigastric pain. He started having a severe pain in the epigastric region about 6 years ago. The pain recurred at varying intervals, but a mild continuous ache persisted. There was tenderness and rigidity between the xyphoid process and the umbilicus. The urine showed (+) sugar; the red blood cell count was 3,800,000; the white blood cell count was 2,500, with a normal differential; and the blood chemistry revealed slightly elevated alkaline phosphatase and a diabetic glucose tolerance curve. Hypotonic duodenography disclosed a double contour of the inner aspect of the second portion of the duodenum with a slight rigidity.

Pancreatogram showed a markedly dilated duct with a narrowing in the area of the head of the pancreas—a finding compatible with carcinoma of the head of the pancreas (Fig. 8). At operation, no carcinoma was apparent, but the entire pancreas was hardened, and biopsy showed advanced fibrosis and chronic pancreatitis.

CASE V. K.Y., 52 years old, entered the Yame Public Hospital on January 3, 1972, as an emergency case complaining of an acute abdominal pain. His past history was unremarkable. On admission, he was in acute distress, and the abdomen was rigid like a board. The red blood cell count was 3,130,000; Hb 9.9 gm. per 100 ml.; white blood cell count, 9,000; and the erythrocyte sedimentation rate was 55 mm./hr. Blood chemistry disclosed a moderate increase in alkaline phosphatase and slight increases in bilirubin and serum amylase. The Pancreozymin-Secretin test carried out after the acute symptoms had subsided, showed reduction in pCO_2 (maximum 102 mEq./L.) and in amylase output; absorption studies disclosed reduced urinary xylose excretion, slightly increased fecal excretion of I^{131} triolein and normal Schilling test.

On a plain abdominal roentgenogram, 2 calcified lesions, one round and the other oblong, were identified along the right side of the third lumbar vertebra. The upper gastrointestinal series showed a round filling defect in the second portion of the duodenum that corresponded with the round calcification (Fig. 9).

Pancreatogram (Fig. 10) revealed 2 stones in a dilated pancreatic duct. The round stone in



FIG. 8. Case IV. Chronic sclerosing pancreatitis. The main duct is markedly dilated, but not so irregular and tortuous as in the previous 2 cases of pancreatic stones. The terminal portion of the duct near the duodenum is suddenly narrowed and it appears as though there is a growth along the duct—a finding highly suggestive of neoplasm. It turned out to be a cirrhotic pancreas.

the accessory duct had apparently increased in size and protruded into the duodenum.

DISCUSSION

The pancreas is an organ which is not readily accessible, and therefore difficult to assess for diagnostic measures of disease.

Hypotonic duodenography has been a relatively recent innovation in the roentgenologic technique, but is far short of a definite advancement.

Retrograde pancreatic ductography, described in this paper, seems promising, and many endoscopists are enthused about its usefulness. Yet, in our limited series of 47 cases, the prior diagnosis was corrected in only 2 instances (Cases I and V) and confirmed in 5 others. In the rest, the procedure did not appreciably contribute to the diagnosis, and, worst of all, it altered the previous correct diagnosis to an incorrect diagnosis in 1 instance (Case IV). The latter case presented a problem of differentiation between chronic pancreatitis with marked narrowing of the duct and less advanced carcinoma of the pancreas. Insertion of the cannula was unsuccessful in advanced carcinomas of the ampullary region that include papillary, choledochal and pancreas head carcinomas. In such instances, duodenoscopy combined with biopsy or brush cytology usually suffices to make the diagnosis.



FIG. 9. Case V. Roentgenogram of the abdomen reveals 2 large calcifications, the round one protruding into the lumen of the second portion of the duodenum. A submucosal growth with calcification was suspected.

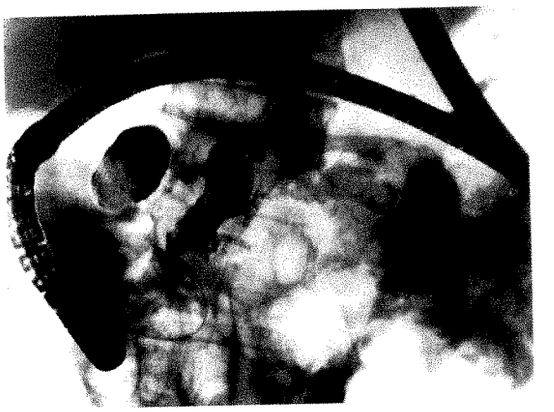


FIG. 10. Case V. Pancreatogram demonstrates dilated and tortuous pancreatic ducts, with increased opacity of the 2 stones due to superimposition of the opaque medium. The oblong stone is in the main duct and the oval stone is in the accessory duct. Obviously, the stone in the accessory duct had become large in size and protruded into the duodenum.

Considering the physical burden and the risk on the part of the patient, endoscopic pancreatography may be warranted or strongly advocated only in a limited number of patients at this moment.

As regards the risk involved, we have measured serum amylase levels prior to and after the procedure at short intervals. It increased in about one-half of the patients within 2–6 hours (Fig. 11). A preventive use of Trasylol seems to be beneficial in suppressing hyperamylasemia, although the amount of contrast medium injected had a more direct bearing on it. Fortunately, we have not yet encountered acute pancreatitis which theoretically could set in, due to the introduction of duodenal content into the pancreatic duct.[1] There has been at least 1

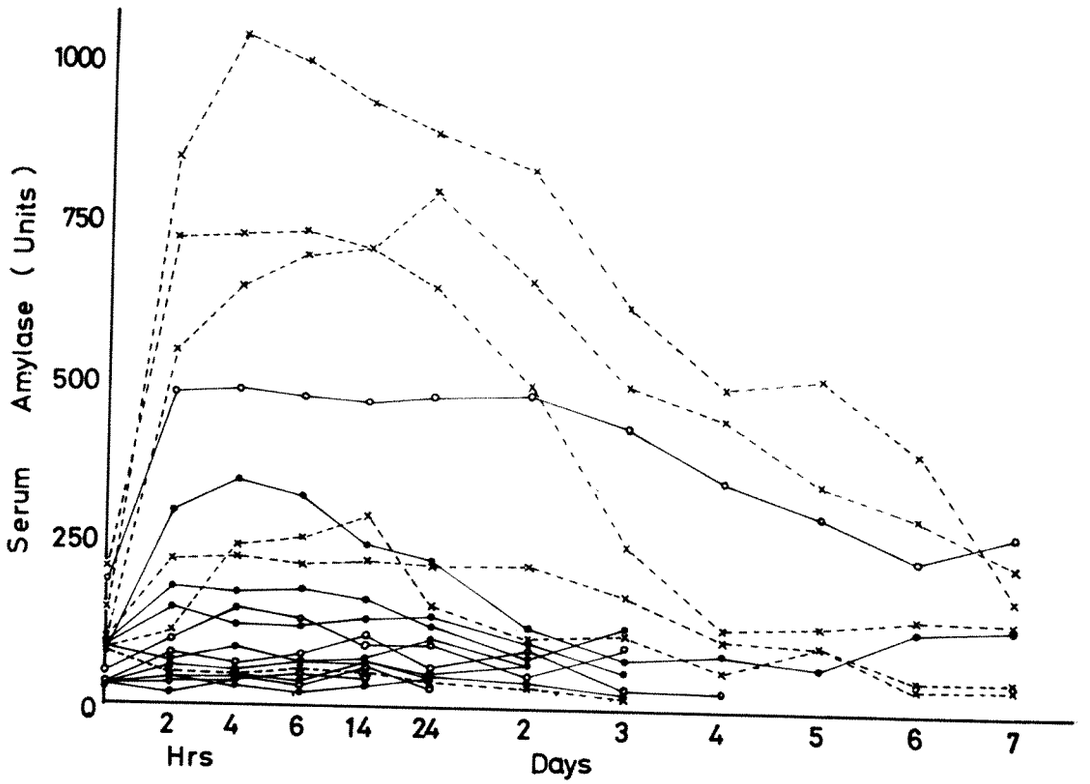


FIG. 11. Serum amylase levels prior to and after retrograde pancreatography, determined in 13 subjects with normal pancreas and 5 cases of chronic pancreatitis. ●——● Normals to whom Trasylol was given as a preventive measure; x- - - -x normals in whom no Trasylol was used; ○——○ chronic pancreatitis cases, no Trasylol used.

accident elsewhere in this country, although not documented, in which biliary peritonitis followed the procedure, probably as a result of an injury to the duct.

Accumulation of clinical data will in due time improve the ability to interpret the ductogram, and early pancreatic carcinoma may be diagnosed from the changes in the duct. Further improvement of the interpretation may be obtained in considering several other parameters, including the length and diameter of the duct, the speed of clearance of the contrast medium, and for that matter, the physiologic variations and changes with age on ethnic grounds.

Because of the inconsistent results, the diagnostic value of retrograde choledochography also seems to be somewhat limited, although in our series, it contributed a great deal to the diagnosis in the cases in which intravenous cholecystography failed to show small stones in the common duct. In a case of a liver carcinoma of the hilar origin, the exact location of the stenosis was determined by retrograde choledochography. This procedure may be of great significance in patients in whom roentgenologic study of the biliary system is imperative, yet transhepatic cholangiography has failed, or has been contraindicated. In general, transhepatic cholangiography involves greater risk than does the retrograde approach.

If, ideally, retrograde pancreatography and cholangiography could be performed without risk and with a high rate of success, endoscopic pancreato-cholangiography could prove to be an indispensable procedure for patients with suspected pancreatic and biliary system diseases.

SUMMARY

Using an Olympus JF-B type fiber-duodenoscope, retrograde pancreatography and/or choledochography has been carried out on 47 subjects.

The Vater papilla was cannulated in 86 per cent of the attempts, and in 83 per cent the pancreatic ductogram was obtained. The common duct was visualized less frequently.

There has been no accident, although in about one-half of the subjects, a transient rise in serum amylase occurred shortly after the procedure, which seemed to be avoided by reducing the amount of contrast medium to be injected and minimized by the preventive use of Trasylol.

Although evaluation of the diagnostic significance of retrograde pancreatography is yet to be determined, it was helpful in the diagnosis of chronic pancreatitis and carcinoma of the pancreas, and may prove to be a reliable measure in patients with suspected pancreas and biliary tract diseases, if carried out properly.

Further improvement in instrumentation, technique and skill may be expected. Accumulation of clinical data is mandatory, at the moment, to improve the interpretation of the ductogram.

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DIFFERENTIAL DIAGNOSIS OF PANCREATIC CALCIFICATION*

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THE tendency for patients with chronic pancreatic disease to develop pancreatic calcification has long been recognized. Graff[25] recorded the presence of pancreatic concretions in 1667, while both Klob[11] and Friedreich[6] noted the association of such calcification with chronic pancreatitis. In 1914 Lacoutre and Charbonnel[12] demonstrated pancreatic calculi in a living patient by means of abdominal roentgenographic examination, and subsequently this roentgenographic finding has become established as one of the most common manifestations of chronic pancreatic inflammation. Despite the development of numerous sophisticated techniques currently employed in evaluation of the pancreas, demonstration of pancreatic calcification on plain abdominal roentgenograms remains the most reliable roentgenologic indication of pancreatic pathology.

In this country, alcoholic pancreatitis is the commonest cause for pancreatic lithiasis. There are, however, a number of less frequent—but interesting and important—etiologic possibilities which should be considered when such calcification is demonstrated roentgenologically.

The purpose of this report is to analyze those clinical and roentgenologic features which aid in differentiating between pathologic conditions capable of producing visible pancreatic calcification.

ALCOHOLIC PANCREATITIS

In the United States pancreatitis occurs mostly in association with biliary tract disease or alcoholism; the former type, however, seldom produces pancreatic calcification. The incidence of pancreatic lithiasis in patients with "gallstone pancreatitis" is only 2 per cent or less.[9] On the other hand, between 20 and 40 per cent of all patients with chronic alcoholic pancreatitis develop intrapancreatic calcific deposits.[7,23] Many clinical series have documented the frequency of alcoholic pancreatitis in patients with pancreatic lithiasis. For example, Sarles *et al.*[23] investigated 55 patients with pancreatic calcification and, of these, 49 (88 per cent) consumed more than 50 gm. of alcohol per day.

Calcification encountered in chronic alcoholic pancreatitis usually develops only after 5 to 10 years of episodic abdominal pain.[9] It consists almost exclusively of intraductal calculi.[15] On histologic examination nearly all apparently intraparenchymal calcification is found to represent the remains of intraductal calculi within areas of surrounding tissue necrosis.[28] Calcifications of this sort appear, roentgenographically, as numerous irregular concretions of varying, but generally small, size deposited throughout the gland (Fig. 1). Calcifications are limited to the head or tail in about



FIG. 1. Chronic alcoholic pancreatitis. Numerous small, irregular concretions of various sizes are deposited throughout the pancreas.

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Fig. 2. Intraparenchymal hemorrhage. Pancreatic angiogram demonstrates aneurysm of transverse pancreatic artery (straight arrow) surrounded by a ring of calcified hematoma (curved arrows). (Courtesy of Dr. Stanley Baum, Boston.)

a quarter of all cases[9] and rarely solitary pancreatic calculi can be identified. True calcification of pancreatic parenchyma can occur after trauma or infarction, where there has been intraparenchymal hemorrhage. In addition, the small intrapancreatic aneurysms which sometimes develop in patients with pancreatitis may bleed with subsequent calcification of the resulting hematoma (Fig. 2).[3] Pancreatic calcification can be observed in from 12 to 20 per cent of all patients who develop pseudocysts as a complication of pancreatitis.[4] Usually the pattern of calcification is similar to that seen in patients with uncomplicated chronic pancreatitis (Fig. 3), but occasionally a rim of calcification outlines the pseudocyst.

HEREDITARY PANCREATITIS

Hereditary pancreatitis is an autosomal dominant disorder characterized by recurrent episodes of abdominal pain usually beginning in childhood and continuing despite all efforts at therapy. More than 100 cases, representing members of over 20 kindreds, have now been reported.[13] No consistent anatomic abnormality of the pancreas, ducts or ampulla has been found in the more than 40 patients who have undergone surgical exploration.

Many patients with hereditary pancreatitis ultimately develop pancreatic cancer—fully 21 per cent of all deaths in patients with this disorder have resulted from pancreatic malignancy. An even higher proportion of these individuals develops pancreatic lithiasis. Thirteen of the 22 patients (59 per cent) studied by Lapey[13] had roentgenographically visible calcifications. The calcifications are typically rounded and are often larger than those found in other pancreatic diseases (Fig. 4). This appearance may allow roentgenologic diagnosis, especially in relatively young, nonalcoholic patients.

HYPERPARATHYROIDISM

It is now well accepted that pancreatitis may occur in association with hyperparathyroidism. The incidence of this occurrence has been estimated to be from 6.5 to 18.9 per cent.[14,24] Although the exact mech-

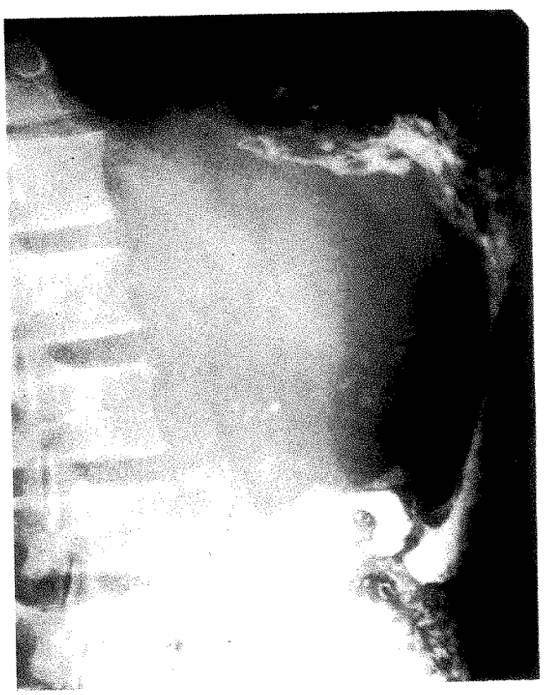


Fig. 3. Pancreatic pseudocyst. Typical pancreatic calcification indicates chronic pancreatitis and permits identification of retrogastric pseudocyst.

anism remains open to question, most authors agree that the former occurs as a result of the latter. This etiologic relationship is substantiated by numerous instances where parathyroidectomy was followed by remission of pancreatitis.[16]

Paloyan *et al.*[18] on the other hand, have suggested that hyperparathyroidism may represent the result rather than the cause of pancreatitis. They have demonstrated hyperplasia of the glucagon-producing alpha cells within the islets of Langerhans of patients with chronic pancreatitis. Hypersecretion of glucagon, in turn, appears to promote hypocalcemia and a reactive functional hyperparathyroidism with associated parathyroid hyperplasia.

Regardless of the exact causal mechanism involved, about half the patients whose hyperparathyroidism is complicated by pancreatitis develop chronic disease and in these individuals pancreatic calcification is frequently detected. This finding was noted in 45 per cent of the 62 patients studied by Mixter *et al.*[16] From published reports there is nothing unique about the pancreatic lithiasis present in hyperparathyroidism, but there is a very high incidence of associated nephrocalcinosis and nephrolithiasis in such cases. Renal calcification was present in 70 per cent of the patients reported by Ludwig and Chaykin[14] regardless of whether or not pancreatic calcification was present. Six patients with hyperparathyroidism and pancreatic calcification studied by Stobbe *et al.*[28] all had a significant degree of nephrocalcinosis. Since pancreatitis may develop before there is any overt evidence of hyperparathyroidism, it is incumbent upon radiologists to suggest the possibility of parathyroid disease whenever renal and pancreatic calcifications are found together.

KWASHIORKOR
(Protein Malnutrition)

In underdeveloped nations of the world, pancreatic calcification is frequently associated with protein malnutrition. The patients involved may develop histologic abnormalities of the pancreatic acinar cells in early childhood and often manifest pancreatic lithiasis before reaching adulthood.[17] Abdominal pain is a less prominent feature than in western patients; this is especially true in Indonesia where none of the patients with pancreatic calcification had abdominal pain.[17] On the other hand, complications such as diabetes and steatorrhea are more common and tend to develop at an early age. In most African and Asian patients there has been no history of alcoholism, but in Uganda many patients with pancreatic calcification have had a history of heavy drinking superimposed on a background of low protein nutrition.[26]

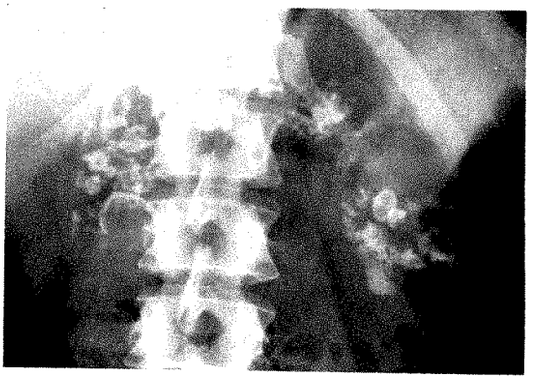


FIG. 4. Hereditary pancreatitis. The calcifications are rounder and larger than those usually found in other pancreatic diseases.

The calcification present in such patients is roentgenographically similar to that seen in western patients with chronic alcoholism, but the historical and geographic factors involved should allow prompt diagnosis.

CYSTIC FIBROSIS

Pancreatic calcification is found at autopsy in many patients with cystic fibrosis and occasionally such calcification may be apparent on abdominal roentgenograms. Reeves and Moran[22] reported such calcification in a patient only 4 years old. Patients with roentgenographically visible pancreatic calcification usually have fairly advanced pancreatic fibrosis associated with diabetes mellitus. The calcification is

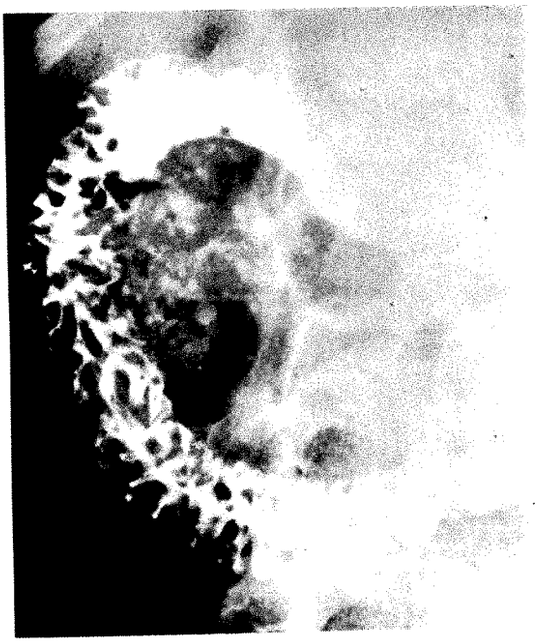


Fig. 5. Cystic fibrosis. Roentgenogram from upper gastrointestinal barium examination reveals finely granular calcifications—mainly in the head of the pancreas. (Courtesy of Dr. Walter Berdon, New York, New York.)

typically finely granular in appearance (Fig. 5); individual calculi are almost invariably smaller than the fairly large deposits which characterize hereditary pancreatitis.[13] These 2 conditions account for the great majority of pediatric pancreatic lithiasis encountered in this country; thus, it is of some interest that the patterns of calcification are often roentgenographically distinct. In most instances, however, the diagnosis of cystic fibrosis will have been made before pancreatic calcification becomes manifest.

IDIOPATHIC PANCREATIC CALCIFICATION

Most series of patients with roentgenographically demonstrable pancreatic calcification include at least a few individuals in whom there have been no clinical manifestations of pancreatic disease.[15] The causes responsible for calcification in these patients are not fully understood. McGeorge *et al.*[15] have suggested that idiopathic pancreatic calcification detected in adulthood may result from subclinical cystic fibrosis in infancy, although this relationship does not appear to explain all cases. Certain alcoholics develop pancreatic lithiasis without other clinical evidence of pancreatitis; but, since the entity of "painless pancreatitis" is well established, these patients are presumed to have pancreatitis despite their lack of symptoms. Stobbe and his associates[28] recently studied histologic material from 22 patients with symptomless pancreatic lithiasis (only 1 was an alcoholic). In each case the calculi were found "upstream" from an area of nonspecific pancreatic ductal obstruction. Pathologically, these patients had ductal dilatation, periductal fibrosis, parenchymal atrophy and fatty replacement in the involved portions of the pancreas. These findings were felt to represent the effects of obstructive atrophy rather than chronic inflammation.

PANCREATIC CALCIFICATION AND PANCREATIC CANCER

There is an increased incidence of pancreatic cancer in patients with chronic pancreatitis.[2,19] This relationship is true for alcoholic pancreatitis and, especially, for hereditary pancreatitis; one-fifth of all deaths which have occurred in patients studied for the latter disorder have been due to pancreatic cancer.[13] The incidence of pancreatic cancer has been reported to be particularly high in patients with pancreatic calcification. Paulino-Netto *et al.*[19] suggested that 20 per cent of all patients with pancreatic lithiasis might have concurrent pancreatic carcinoma. Subsequently, Johnson and Zintel[10] reviewed 677 cases and found only 24 (3.7 per cent) with coexisting carcinoma. Conversely, in 2 recent studies of patients with pancreatic cancer, only 3 of 183 (1.6 per cent) had pancreatic lithiasis.[2,21] A consideration of these statistics indicates that benign disease will be present in over 95 per cent of all patients with roentgenologically demonstrable pancreatic lithiasis. Thus, while the incidence of pancreatic cancer in patients with pancreatic calcification is very significantly

higher than that for the general population, this roentgen finding should still be considered an indicator of benign rather than malignant pancreatic disease.

In those uncommon instances where pancreatic cancer and pancreatic lithiasis coexist, the calcium usually represents the effect of pre-existent pancreatitis and is diffusely present throughout the gland. In occasional instances, however, malignant pancreatic ductal obstruction has produced lithiasis restricted to that portion of the organ upstream from the obstruction.[28]

In one widely publicized instance, pancreatic calculi secondary to chronic pancreatitis were observed to disappear in a patient who later developed pancreatic carcinoma.[29] This same phenomenon (*i.e.*, disappearing calcification) has been noted in patients with chronic pancreatitis alone,[3] and along the same lines, displacement of pre-existing calcification may define the growth of pseudocysts (Fig. 6).[1]



FIG. 6. Pancreatic pseudocyst. Anteroposterior tomogram reveals displacement of pre-existing pancreatic calcification (arrows) by rounded, noncalcified, space-occupying lesion. The cystic nature of the lesion was revealed by ultrasonography and confirmed at surgery.

TUMOR CALCIFICATION

For all practical purposes, adenocarcinoma of the pancreas is not associated with tumor calcification. Actual tumor calcification does occur, however, in approximately 10 per cent of patients with cystadenoma or cystadenocarcinoma of the pancreas.[20] In many instances the calcification found in such tumors is nonspecific in its roentgenographic appearance, but occasionally a radiating "sunburst" pattern is present.[18] This configuration correlates with gross pathologic findings where cystic spaces are seen to separate spoke-like stromal elements which radiate from a central nidus. When such calcification is observed, a specific plain film roentgenographic diagnosis can be made (Fig. 7, *A* and *B*).

One other rare pancreatic tumor, the cavernous lymphangioma, calcifies and again the pattern of calcification may allow plain film roentgenographic diagnosis. In such cases a collection of phleboliths in and adjacent to the pancreas is the characteristic feature.[5]

SUMMARY

Roentgenologically demonstrable pancreatic lithiasis may occur in a number of conditions. In this country about 90 per cent of the patients in whom such calcification is shown will have *alcoholic pancreatitis*. A history of longstanding alcoholism with frequent episodes of severe abdominal pain can usually be obtained from such patients.

Hereditary pancreatitis may be suspected roentgenologically when large, unusually rounded pancreatic calculi are demonstrated. A positive family history is the most important diagnostic element in such cases.

When pancreatic lithiasis occurs in association with nephrocalcinosis, *hyperparathyroidism* should be suspected and the appropriate chemical studies performed.

A few patients with advanced *cystic fibrosis* and diabetes mellitus have roentgenologically evident pancreatic calcification.

In underdeveloped nations, pancreatic calcification is frequently observed in association with *protein malnutrition*; whether such calcification occurs in impoverished

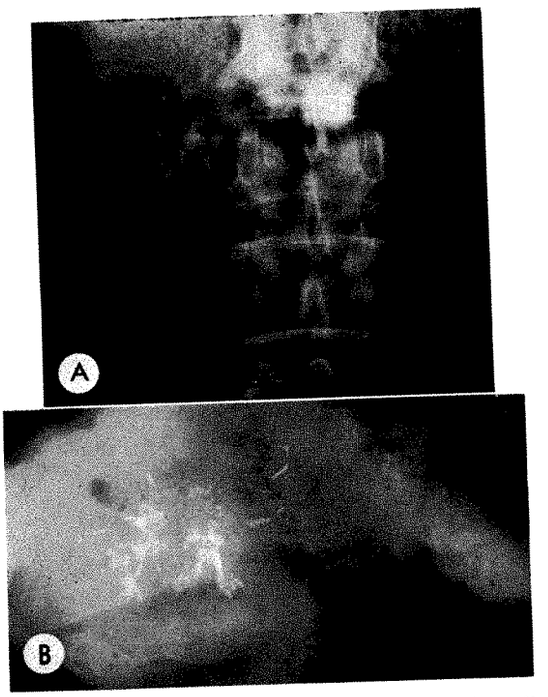


Fig. 7. Cystadenocarcinoma. (*A*) Typical "sunburst" pattern of calcification in the head of the pancreas. (*B*) Roentgenogram of surgical specimen accentuates the pattern of calcification.

sections of the United States is not known.

From 2 to 4 per cent of all American patients with pancreatic calcification have coexisting *pancreatic carcinoma;* it appears that alcoholism and chronic pancreatitis in some way predispose to development of pancreatic malignancy. When calcification occurs together with pancreatic cancer, it usually indicates pre-existing pancreatitis. Occasionally it is present only proximal to a tumor which has occluded the pancreatic duct and these patients may not have had any previous pancreatitis.

Actual tumor calcification may occur in *cystadenoma* and *cystadenocarcinomas.* In some of these cases a radiating spoke-like pattern allows preoperative diagnosis.

Cavernous lymphangioma is another neoplasm in which the pattern of calcification may be characteristic.

In occasional instances pancreatic lithiasis occurs in patients without any clinical evidence of pancreatic disease. Such patients usually have *nonspecific pancreatic ductal stenosis* with formation of calculi upstream from the site of obstruction.

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EDITORIALS

OF DOGS AND FROGS AND CHOLECYSTOKININ

HIPPOCRATES believed that black bile was associated with melancholy; and some hospital medical audit committees feel that cholecystectomy in the absence of stones is suspect. Both opinions are probably wrong, but each is backed by the weight of considerable, although not necessarily similar, authority. Hippocrates' opinion may rest with him; but work is now being done to permit accurate preoperative diagnosis of chronic acalculous cholecystitis and thus to alleviate another source of significant, though undramatic, disease.

Recently, Nathan *et al.*,[1] by using cholecystokinin cholecystography, have detailed steps in identifying patients with chronic cholecystitis, subsequently proved surgically, in whom the usual cholecystogram was normal.

In 1928 Ivy and Oldberg[2] identified a hormone, cholecystokinin, elaborated by the duodenal mucosa, which produces contraction of the gallbladder in dogs. This hormone was found to be active in humans as well, and within 2 years of its discovery the clinical use of cholecystokinin in man was reported by Ivy, Drewyer, and Orndoff,[3] the latter one of the founders of the Radiological Society of North America. Unfortunately, the material then available led to undesirable side effects. The standards of pharmacologic activity were established in relation to the response of the biliary tract of the dog, and this activity is expressed in Ivy dog units.

Workers in Sweden, and particularly Jorpes and Mutt,[4] have purified cholecystokinin, and have produced a material much more concentrated. This purified cholecystokinin has few and mild side effects. Much of what was used clinically has come from Jorpes and Mutt,[4] and more than 250,000 doses have been administered without untoward effect.

In 1967 it was found that a methanol extract of the skin of an Australian tree frog, *Hyla caerulea*, has a much more vigorous effect on the gallbladder than cholecystokinin itself.[5] Cholecystokinin is a linear polypeptide containing 33 amino acids. Caerulean, the frog skin extract, is a polypeptide of 10 amino acids, and has the same carboxyl terminal as cholecystokinin. On analysis, it appears that a heptapeptide fraction of the cholecystokinin molecule and a heptapeptide fraction of the caerulean are almost identical. Further, the pharmacologic action on the gallbladder and small intestine appears to reside in this fraction, or in a similar octapeptide fraction, also ending in a carboxyl radical.

This octapeptide fraction has been recently synthesized by Ondetti and his co-

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workers.[6] The relative activity can now be measured in weight instead of the previously used Ivy dog units. The pharmacologic effect of 100 dog units is represented by 4 milligrams of pure cholecystokinin, and 33 nanograms of either the purified frog skin extract or the synthetic octapeptide.

The physiologic activity of cholecystokinin and its synthetic portions is complicated but forms the basis for its use. Injection of the substance is followed within minutes by contraction of the gallbladder and simultaneous relaxation of the sphincter of Oddi. Increase in the tonus of the pyloric sphincter occurs, the oral half of the duodenum relaxes, and the aboral half develops increase in tonicity, with increased peristaltic activity. Subsequently, the remainder of the small intestine also shows increased peristalsis, with considerable shortening of the transit time to the cecum. Although the onset of effect is rapid, and peak activity occurs within 15 minutes, the stimulus persists for about 90 minutes, depending on the dose. There are additional effects on gastric secretion, and these vary according to whether gastrin or histamine is present.

Cholecystokinin has been used in clinical medicine to improve barium studies of the small intestine.[7] After barium administered by mouth has reached the aboral half of the duodenum, injection of 33 nanograms of cholecystokinin per kilogram of body weight permits examination of the entire small intestine in a period of about 20 minutes. Because of the effect on the pyloric sphincter and the paradoxical effect on the oral half of the duodenum, it is necessary to withold the stimulus until the meal has passed into the aboral duodenum. It has been shown by Parker and Beneventano[8] that all lesions shown with the conventional study are also well shown in the accelerated examination. This method may be of additional value in investigating otherwise unexplained prolongation of transit time.

A possibly more significant use is that reported by Nathan *et al.*,[1] in the examination of the gallbladder. In patients who have shown normal function and appearance of the gallbladder by previous routine cholecystography, these radiologists have been able to make a roentgenographic diagnosis of chronic cholecystitis, by noting the response of the opacified gallbladder to injection of cholecystokinin. Further, they were able to identify those patients who would be relieved of symptoms after cholecystectomy. Their report presents 141 patients and an equal number of controls. Of 79 with abnormal cholecystokinin cholecystograms, 77 were proved to have chronic cholecystitis at operation. This pathologic material was reviewed by 2 pathologists. The operated patients have been followed for a period between 3 and 48 months. It is worthy of note that in 25 per cent of their patients, the gallbladder appeared normal at the time of operation, but the combination of abnormal cholecystokinin cholecystogram, abnormal histology, and clinical cure seems convincing as to the value of their method.

Other physicians have used the cholecystokinin cholecystogram for demonstration of small stones, not otherwise visible, and for visualization of the cystic and common ducts during conventional cholangiography, thus decreasing the need for additional preoperative cholangiography.

The side effects of the injection are few. Occasionally, nausea occurs for a few minutes after injection. At times, there is intestinal cramping, due to the effect on the small intestine.

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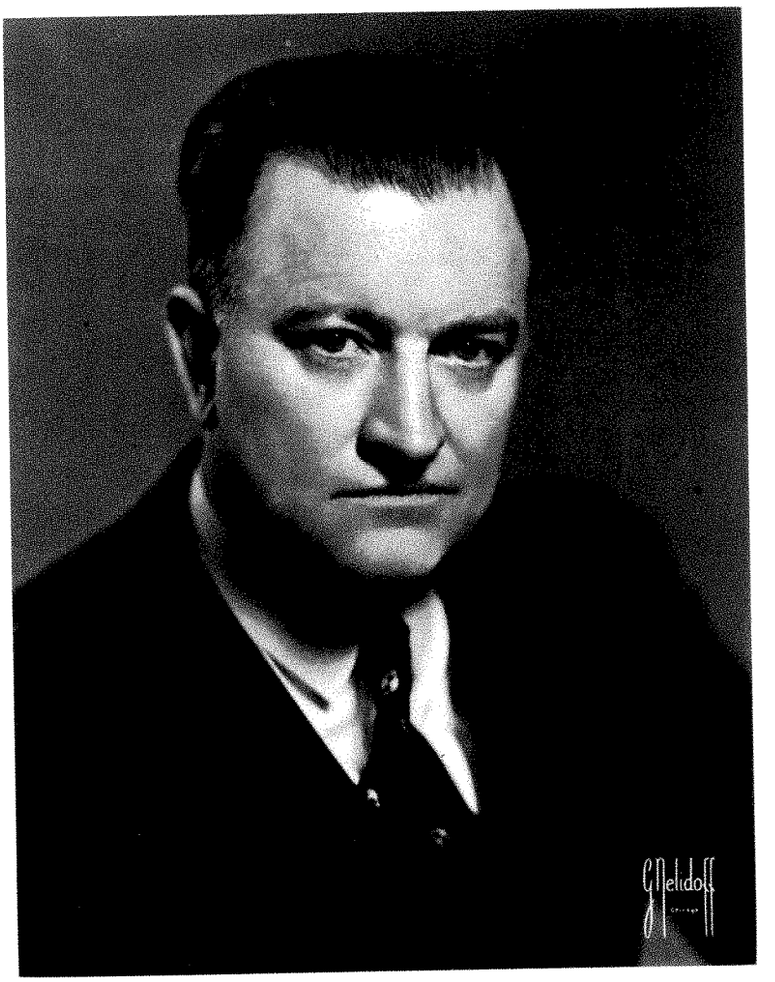
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It has been found that injection of cholecystokinin after administration of food at the usual meal time induces unusual somnolence in the cat.[9] Cholecystokinin is released from the duodenum when the latter is stimulated by the presence of fat in its lumen. This release of cholecystokinin may account for 2 well known, but not entirely laudable responses: the drowsiness of the medical student at his first after-lunch lecture; and the occasional somnolence which greets the after-dinner speaker. Both responses are probably potentiated by large amounts of natural cholecystokinin.

E. Frederick Lang, M.D.

[9] Fara, J. W., Rubinstein, E. H., and Sonnenschein, R. R. Visceral and behavioral responses to intraduodenal fat. *Science*, 1969, *166*, 110–111.



EDWARD LELAND JENKINSON, M.D.
1892–1972

EDWARD L. Jenkinson died early Sunday morning, July 30, in St. Mary's Hospital, Rhinelander, Wisconsin, the town of his birth, at the age of 80 years. Although in the last ten years of his life Dr. Jenkinson was plagued with several illnesses necessitating surgery, the immediate cause of death was cerebral hemorrhage.

Dr. Jenkinson was born in Rhinelander on February 25, 1892, but his parents moved to Minocqua when he was at an early age. There he owned a home since 1925. Following graduation from Minocqua High School he attended Marquette then St. Louis University, where he graduated with a B.S. degree in 1910 and M.D. degree in 1915. He interned at Alexian Brothers and St. Luke's Hospitals in St. Louis, 1914–1915. He then returned to Minocqua for a short time, assisting the pioneer Dr. Torpy in his practice, followed by an appointment to the medical staff at St. Luke's Hospital, Chicago, in 1916, and rapidly advancing to Director of the Department of Radiology.

In addition he was Director of the Departments at St. Joseph's Hospital, 1923–1939; Evanston Hospital, 1923–1929; and Ravenswood Hospital. Dr. Jenkinson's postgraduate work in radiology included: training at St. Luke's Hospital and Battle Creek Sanitarium, under the preceptorship of Dr. James T. Case; courses at Cornell University; and tours of training in Germany and France.

Following 18 months of military service in World War I, A.E.F., with advancement to Major, Dr. Jenkinson married Margaret Parkinson in 1919, a graduate nurse at St. Luke's, who died in 1945. To them was born a daughter, Carol, wife of a physician, Dr. James Bolger, Waukesha, Wisconsin. In 1948 he married Helen Welch Snapp, a devoted and faithful wife and companion who ably supported him in illness. Both Margaret and Helen shared in full measures the honors and contributions of their husband.

Early in his distinguished career Dr. Jenkinson became interested in academic and organized medicine, particularly radiology. His dedication, activities and untiring efforts are well known and will be long remembered. His professional and academic activities involved St. Luke's Hospital and Northwestern University Medical School from 1920 to retirement in 1958. He was appointed to the Northwestern faculty as an Instructor in 1920, and successively advanced through the ranks to Professor in 1947, Chairman of the Department from 1947–1957, and Emeritus Professor in 1957. Throughout these years of academic service his dedicated activities were in the areas of improved undergraduate teaching and residency training.

"Jenk," as he was affectionately known among his colleagues and friends, was a member of many societies—local, state and national. He held many important positions. The following are some that characterize his distinguished career.

In 1921 "Jenk" became a member of the American Roentgen Ray Society, served as Vice President in 1927, Treasurer 1932–1937, President in 1939, and Life Member in 1958. He received the Caldwell Gold Medal and delivered the Caldwell Lecture, "Pyloric Antrum of the Stomach" in 1954. As President he initiated the significant Refresher Courses at the Annual Meetings.

He was one of the founders of the American Board of Radiology in 1932, a member of the first Board of Trustees in 1933, and served until 1960, the longest period of service of any Trustee. All other founders and first Trustees preceded him in death. He served as President from 1946–1948. The dedication and devoted efforts of Ed Jenkinson in the formation and services over a period of 27 years to the American Board of Radiology represent a truly remarkable contribution to radiology.

Membership and activities in other societies include—Fellow and Past-President, Chicago Roentgen Society; Fellow of the Institute of Medicine of Chicago; for many years active in the Section of Radiology of the A.M.A.; Member R.S.N.A.; Honorary Member of the Mexican Radiological Society and the Minnesota Radiological Society; Emeritus Fellow, Past-Treasurer, Past-Member of the Board of Chancellors of the American College of Radiology. He was listed in *Who's Who in America* for many years.

Ed Jenkinson's interest in medicine, particularly radiology, was contagious, with one brother a radiologist, two brothers in the commercial areas of radiology, his daughter the wife of a physician, and a grandson in medical school at Northwestern.

After his retirement, partially due to health problems, and possibly too early as he had much to contribute, "Jenk" spent the summers in Wisconsin and the winters in Florida. He became active in local affairs at Minocqua, Wisconsin, as a member of the American Legion Post, Masonic Lodge and as founder and Past-President of the Minocqua Township Improvement Association. He is survived by his wife, Helen; one daughter, Mrs. James (Carol) Bolger; three brothers, Dr. David, a radiologist in

Chicago, George and Herbert; one sister, Mrs. Tekla Kearns; and three grandchildren.

Ed Jenkinson's life was replete with activity, achievements and contributions to radiology—an outstanding radiologist highly esteemed by his colleagues as a consultant, highly regarded by his employees and residents. The writer will always be grateful and deeply appreciative of his counsel and guidance in organized radiology. All of us fortunate enough to come under his influence and to know him, feel a deep sense of loss at his passing. He will be sorely missed both professionally and personally by a host of friends and colleagues.

Earl E. Barth, M.D.

670 North Michigan Avenue
Chicago, Illinois 60611



KENNETH EDWARD HODGE, D.M.R.D.
1921–1972

WITH the death of Dr. Kenneth Edward Hodge on October 1, 1972 after a long and disabling illness, many of us lost a cherished friend and colleague and McMaster University and the Hamilton Civic Hospitals an exceptionally skilled and competent academic radiologist, teacher and administrator.

He was born on December 7, 1921, in Tunbridge Wells, Kent, England and received his premedical and medical education at Guys Hospital Medical School, London, England, where he graduated with an M.B. and B.S. in 1947. He served as a House Surgeon and House Physician at the Kent and Sussex Hospital and at the Chase

Farm Hospital in England from 1947 to 1949, when he returned to Guys Hospital for postgraduate training in Radiology. He served as a Junior Registrar at Guys Hospital and then as a Registrar at the Radcliffe Infirmary Department of Radiology, Oxford, England, from 1949 to 1951 and received the D.M.R.D. (London) in 1950. In 1952, Prof. J. F. Brailsford, at the University of Birmingham, England, arranged for him a Radiological Fellowship to travel to the United States, which initially took him to Dallas, Texas to work under Dr. J. R. Maxfield, Jr. During the course of his travels and studies, Dr. Hodge first came to Toronto in 1953 and decided to make his home in Canada. He joined the Department of Radiology, of the University of Toronto as a Senior Resident in 1953. During the same year he was certified in Diagnostic Radiology by the Royal College of Physicians and Surgeons of Canada, and obtained the Fellowship of the Royal College of Physicians and Surgeons in 1955. In 1954 he became an assistant radiologist at the Toronto General Hospital and a Clinical Teacher of Radiology at the University of Toronto. In 1956 he became First Assistant to the Director of the Department of Radiology, Hospital for Sick Children and Assistant Professor of Radiology at the University of Toronto. In 1957 he was appointed Chief Radiologist, Sunnybrook Hospital, Toronto, where he remained until 1960. In 1961, he moved to Hamilton, Ontario, and became Director of the Department of Radiology at the Henderson General Hospital, Hamilton. At the same time he joined the ranks of the Faculty of the new medical school at McMaster University as Associate Clinical Professor of Diagnostic Radiology, and held these positions until the time of his death.

Dr. Hodge spared no time or effort in the struggle to develop the Radiological Departments with which he was associated. Under his leadership, organizations and installations to meet advanced and modern radiological needs were emphasized. His keen interest in Obstetrical Radiology is reflected in his publications. Since 1967 he pioneered the introduction of Ultrasound in Obstetrical Radiology at McMaster University and at the Hamilton Civic Hospitals and did extensive work to improve equipment, methods and accuracy of examinations. His efforts were eventually interrupted by his long and unfortunate illness. Even then, he continued his work up to the time of his death.

Dr. Hodge was a gifted and dedicated teacher. Beyond his academic appointments he was active as a faculty lecturer of the Section of Instructions of the American Roentgen Ray Society, where he served in 1956, 1957 and 1958. He served as a lecturer at the Annual Pre-Fellowship refresher courses of the Faculty of Medicine of the University of Toronto and was much sought after as a guest lecturer at the local medical societies. Since 1967, Dr. Hodge materially contributed to the establishment of an entirely new medical curriculum at the new Medical School at McMaster University.

Dr. Hodge was a Fellow of the Royal College of Physicians and Surgeons of Canada; a member of the Canadian Association of Radiologists and of the American Roentgen Ray Society to which he was elected in October of 1958. He was a member of the British Institute of Radiology; the Toronto Radiological Society; a member of the Canadian Medical Association; Ontario Medical Association; the British Medical Association and was active in the Hamilton Academy of Medicine. During the years preceding his death, he joined the American Institute of Ultrasonics in Medicine, in which he took particular interest.

From 1940 to 1941, Dr. Hodge served in the R. A. F. and sustained injuries during wartime service, which in later years led to his disabling and terminal illness. From 1953 to 1960 he served with the R.C.A.F. Auxiliary as a Squadron Leader.

Dr. Hodge was an energetic sportsman during his active years. In his leisure time he was an expert and successful sailor who was keenly interested in keelboat racing

and also an excellent pilot and much interested in light plane flying.

In 1955 he was married to Annamarie Bakker. He was devoted to his family and it is characteristic that he listed the bringing up of his three boys as one of his favorite hobbies. He is survived by his wife and three sons, Derek, Hans and Robert.

We who knew him well, remember him for his enthusiasm, for his energy and for his unique and refreshing sense of humor, and all his colleagues will remember him for his efforts in the practice of high principles and ethics of radiology, as a devoted teacher and as a man of dedicated interest in his specialty.

Dr. Hodge's many friends and associates join in offering condolences to his family.

H. O. Stolberg, M.D., F.R.C.P.(C)

Department of Diagnostic Radiology
Hamilton Civic Hospital
237 Barton Street, East
Hamilton 21, Ontario
Canada

NEWS ITEMS

NEW OFFICERS OF THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

At the Fifty-eighth Annual Meeting of the Radiological Society of North America held November 26–December 1, 1972 at the Palmer House in Chicago, Illinois, the following officers were elected: *President*, David S. Carroll, M.D., Memphis, Tennessee; *President-Elect*, Robert D. Wise, M.D., Boston, Massachusetts; *First Vice-President*, John C. Bennett, M.D., San Francisco, California; *Second Vice-President*, William T. Moss, M.D., Wilmette, Illinois; *Third Vice-President*, Robert B. Quattelbaum, M.D., Valdosta, Georgia; *Secretary*, Hillier L. Baker, Jr., M.D., Rochester, Minnesota; *Treasurer*, Harold O. Wyckoff, Ph.D., Rockville, Maryland; and *Historian*, Howard P. Doub, M.D., Detroit, Michigan.

The *Chairman of the Board of Directors* is John W. Beeler, M.D., Indianapolis, Indiana.

The Gold Medal of the Society was awarded to Harold G. Jacobson, M.D., New York, New York; and Lucy Frank Squire, M.D., New York, New York.

The Fifty-ninth Annual Meeting of the Society will be held at the Palmer House in Chicago, Illinois, November 25–30, 1973.

FIFTIETH ANNIVERSARY OF THE CLEVELAND RADIOLOGICAL SOCIETY

The Cleveland Radiological Society announces that it will celebrate the 50th anniversary of its founding with a meeting on the afternoon of Saturday, March 24, 1973. The speakers for the meeting will be Dr. Sidney Nelson, Dr. William Martel and Dr. Morris Simon. There will be a banquet that evening which will be addressed by Dr. Simon.

It is believed that this society is one of the oldest local radiology groups in the country. Former members who once practiced in Cleveland are cordially invited to return for the meeting.

Further information can be obtained from the Co-chairmen, Dr. Fred Rose, University Hospitals, or Dr. George Krause, Mt. Sinai Hospital, Cleveland, Ohio 44106.

ADVANCES IN LYMPHOGRAPHY

A "Postgraduate Course in Radiology," presented by the Department of Radiology, University of Arizona College of Medicine, Tucson, Arizona; with a Distinguished International Guest Faculty, organized by M. Paul Capp, M.D., University of Arizona, P. Ruben Koehler, M.D., University of Utah, and Manuel Viamonte, Jr., M.D., University of Miami, will be held March 3–5 (noon), 1973, just before the 4th International Congress of Lymphology, already announced for March 6–10, 1973 (see October 1972 issue of Journal, p. 449).

For further information please write to M. Paul Capp, M.D., Professor and Chairman, Department of Radiology, College of Medicine, The University of Arizona, Arizona Medical Center, Tucson, Arizona 85724.

SEMICONDUCTOR DETECTORS IN MEDICINE

A symposium to highlight the growing applications of semiconductor detectors in clinical and investigative medicine will be held at Hyatt House, Union Square, San Francisco, California, March 8–9, 1973.

A distinguished Guest Faculty of 15 authorities will participate.

For information please write to Leon Kaufman, Ph.D., or David C. Price, M.D., Department of Radiology, University of California, San Francisco, California 94122.

AMERICAN CANCER SOCIETY'S NATIONAL CONFERENCE ON UROLOGIC CANCER

The American Cancer Society will hold the National Conference on Urologic Cancer at the Shoreham Hotel, Washington, D.C., March 29–31, 1973.

The objective of this conference is to summarize the present knowledge in the field of urologic neoplasms for an interdisciplinary audience including the general practitioner, internist, surgeon, pediatrician, radiologist and urologist.

The sessions are open to all members of the medical and related professions. Advance registration is requested.

The Conference is being held in cooperation with the American Urological Association, American College of Surgeons, American Society of Therapeutic Radiologists, and American Academy of Pediatrics.

Programs, advance registration cards and hotel reservation cards may be obtained from the Divisions of the American Cancer Society or from: Sidney L. Arje, M.D., National Conference on Urologic Cancer, c/o American Cancer Society, 219 East 42nd Street, New York, New York 10017.

POSTGRADUATE COURSE ON GI TRACT

The Department of Radiology, Cornell University Medical College, will give a "Postgraduate Course on GI Tract," April 9–12, 1973, at the Memorial Hospital Auditorium, 424 East 68th Street, New York, New York.

The Cornell University Medical College and The New York Hospital–Cornell Medical Center Faculty for this course will consist of Drs. John A. Evans, Norman B. Javitt, David C. Levin, Morton A. Meyers, Zuheir Mujahed, D. Gordon Potts, Jeffrey Rothman, George Stassa, Harry L. Stein, Robin C. Watson, Joseph P. Whalen, and Patricia Winchester.

The Guest Faculty will include Drs. Stanley Baum, Arthur R. Clemett, Henry Colcher, Shelby Galloway, Heisaburo Ichikawa from Tokyo, Japan, Mansho T. Khilnani, Richard Marshak, Maurice M. Reeder, Ralph Schlaeger, Solomon S. Schwartz, Hiromi Shinya, William B. Seaman, Jack A. Vennes and Bernard Wolf.

For application for enrollment please write to: John A. Evans, M.D., Department of Radiology, Cornell University Medical College, 1300 York Avenue, New York, New York 10021.

WORKSHOP IN RENAL RADIOLOGY

The Department of Diagnostic Roentgenology of the Mayo Clinic is sponsoring a "Workshop in Renal Radiology" on May 16–18, 1973.

Emphasis will be centered on techniques of urography and the practical radiologic approach to renal disease. Attendance will be limited to 30.

The visiting faculty will include C. J. Hodson, M.D., Anthony F. Lalli, M.D., and David M. Witten, M.D. Members of the Mayo Clinic staff will also participate.

Further information and applications may be obtained by writing: Continuing Education—Workshops in Radiology, Department of Diagnostic Roentgenology, Mayo Clinic, Rochester, Minnesota 55901.

POSTGRADUATE COURSE ON RADIOLOGY OF THE GASTROINTESTINAL TRACT AND URINARY TRACT

The Department of Radiology, State University of New York, Downstate Medical Center will sponsor a "Postgraduate Course on the Radiology of the Gastrointestinal Tract and Urinary Tract," May 28th to June 1st, 1973.

The material will be presented both in seminar format, with a maximum of 12 registrants participating with individual faculty members, and in classical lecture format. The faculty will include: J. Becker, W. Berdon, E. Boijsen, S. Boley, M. Bosniak, A. R. Clemett, J. Farman, E. Friedman, C. J. Hodson, M. Khilnani, A. Lalli, E. McNally, P. E. S. Palmer, C. Plimpton, J. Rabinowitz, T. Robinson, S. Schwartz, H. Spiro, K. Waterhouse and D. Witten.

For further information please contact: Department of Radiology, State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, New York 11203.

SYMPOSIUM ON RECENT ADVANCES IN DIAGNOSTIC RADIOLOGY AND NUCLEAR MEDICINE

The First Annual "Symposium on Recent Advances in Diagnostic Radiology and Nuclear Medicine," sponsored by the Department of Radiology of The Johns Hopkins Medical Institutions, will be held at the Turner Auditorium of The Johns Hopkins Hospital, May 29–31, 1973.

The Guest Faculty will include: Drs. W. Alexander, S. Baum, D. Davis, R. Marshak, G. Potter, and E. Theros.

For further information please contact Dr. Frederick P. Stitik, Department of Radiology, The Johns Hopkins Hospital, Baltimore, Maryland 21205.

NATIONAL ACADEMY OF SCIENCES

A National Academy of Sciences advisory committee report, analyzing current scientific knowledge of health risks from ionizing radiation exposure, was made public by the Environmental Protection Agency (EPA). The report is called "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation."

The report presents: analyses of ionizing radiation sources and population exposures to those sources; the modes by which radioactive materials are transported in the environment and their effects; the genetic effects of ionizing radiation; the effects of ionizing radiation on human growth and development; and the somatic effects of ionizing radiation.

Preparation of the report was started under the guidance of the Federal Radiation Council, whose function was transferred to the Environmental Protection Agency in December 1970. The cost of preparing the report was shared by EPA and the Department of Health, Education, and Welfare.

Copies of the report are available for public viewing in Room 611, 1835 K Street, N.W., Washington, D. C. Additional copies of the report have been available since early December, 1972. Single copies may be obtained upon request to the Public Inquiries Branch, Office of Public Affairs, Environmental Protection Agency, Room 206, Waterside Mall, Washington, D. C. 20460. Additional copies may be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, D. C. 20401.

INTER-AMERICAN COLLEGE OF RADIOLOGY

The President of the Inter-American College of Radiology, Dr. Miguel Dao, of Caracas, Venezuela, announces the creation of 3 annual prizes to be awarded by the Inter-American College. One prize is of $1000.00 and 2 prizes of $500.00 each.

The prizes will be awarded for: (1) the best work on research in Radiodiagnosis: (2) the best work on Radiotherapy and Nuclear Medicine; and (3) the most original work containing research and procedures in Radiodiagnosis of the Biliary Tract.

Only members of the Inter-American College of Radiology may participate in the contest. The papers submitted will be published in the *Revista Interamericana de Radiología*, which is the official organ of the Inter-American College of Radiology.

Further details in reference to the contest may be obtained directly from: Dr. Miguel Dao, President, Inter-American College of Radiology, Apartado Postal 14213, Candelaria Caracas, Venezuela, S.A.

BOOKS RECEIVED

BOOKS RECEIVED

The Radiological Clinics of North America. December, 1972, Volume X, No. 3. Symposium on Chronic Renal Disease and Uremia. Guest Editors, Marvin Haskin, M.D., and George Teplick, M.D. Cloth. Pp. 184, with many illustrations. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1972.

A Concise Textbook of Radiotherapy. By Priscilla Barnes, M.B., B.S., D.M.R.T., C.R.C.P. (C), and David Rees, M.Sc., A.F.I.M.A., F.Inst.P. Cloth. Pp. 384, with 86 figures. Price, $22.00. J. B. Lippincott Company, East Washington Square, Philadelphia, Pa. 19105, 1972.

Radioterapia Ginecologica. By Mario Lenzi, Direttore, and Renato Bergonzini, Aiuto universitario, Istituto de Radiologia dell'Università di Modena. Cloth. Pp. 282, with many figures. Edizioni Minerva Medica, 1972.

Protection against Ionizing Radiations. A Survey of Current World Legislation. Paper. Pp. 328. World Health Organization, Geneva. In U.S.A., The American Public Health Association, Inc., 1015 Eighteenth Street, N.W., Washington, D. C. 20036, 1972.

Dynamic Aspects of Brain Scanning. By Jyoji Handa, M.D., Instructor, Department of Neurosurgery, Kyoto University Medical School, Kyoto, Japan. Cloth. Pp. 169, with 136 figures. Price, $22.50. University Park Press, Chamber of Commerce Building, Baltimore, Md. 21202, 1972.

Current Concepts in Radiology. Edited by E. James Potchen, M.D., Professor, Department of Radiology, and Chief, Diagnostic Radiology, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Mo. Cloth. Pp. 346, with 502 illustrations. Price, $24.74. C. V. Mosby Company, 11830 Westline Industrial Drive, St. Louis, Mo. 63141, 1972.

Pediatric Neuroradiology. By Anthony J. Raimondi, M.D., Professor and Chairman of Neurosurgery and Professor of Anatomy, Northwestern University Medical School; Chairman of Neurosurgery, Children's Memorial Hospital, Chicago, Ill. Cloth. Pp. 716, with 988 figures. Price, $45.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1972.

Archives Françaises des Maladies de l'Appareil Digestif. Ninth International Congress of Gastroenterology, Paris, July 5–12, 1972. Paper. Pp. 413. Masson & Cie, 120 Boulevard Saint-Germain, Paris, 1972.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 25–28, 1973.

American Radium Society
Secretary, Dr. Felix N. Rutledge, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025. Annual Meeting: Broadmoor Hotel, Colorado Springs, Colorado, April 22–26, 1973.

Radiological Society of North America
Secretary, Dr. Hillier L. Baker, Jr., Mayo Clinic, Rochester, Minn. 55901. Annual Meeting: Palmer House, Chicago, Ill., November 25–30, 1973.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago, Ill. 60606. Annual meeting: San Francisco, Calif., April 2–7, 1973.

Section on Radiology, American Medical Association
Secretary, Dr. Antolin Raventos, Davis, Calif. Annual Meeting: New York, N. Y., June 24–28, 1973.

American Board of Radiology
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler East, Rochester, Minn. 55901.

Oral examinations will be held in the following cities during the next year: Chicago, Ill., June 4–8, 1973, Marriott Motor Hotel; and Dallas, Tex., Dec. 3–7, 1973, Statler Hilton Hotel.

Written examinations are scheduled in 13 large centers.

Applications must be received in the Board Office before Sept. 30 of the year preceding the one in which the candidate wishes to be examined.

Deadline for filing applications for any examination in 1973 was September 30, 1972.

American Board of Nuclear Medicine, Inc. A Conjoint Board of the American Boards of Internal Medicine, Pathology and Radiology and sponsored by the Society of Nuclear Medicine.
Chairman, Dr. Merrill A. Bender, Suite 2402, 211 E. 43rd St., New York, N. Y. 10017.

Examination for certification in the Specialty of Nuclear Medicine will be given April 7, 1973. The deadline for filing application forms was January 1, 1973.

American Association of Physicists in Medicine
Secretary, D. John Wright, Ph.D., Department of Radiology, Temple Univ. Health Sciences Center, Philadelphia, Pa. 19140. Annual Meeting in San Diego, Calif., July 29–Aug. 3, 1973.

American Society of Therapeutic Radiologists
Secretary, Dr. Herman D. Suit, Radiation Medicine, Massachusetts General Hospital, Boston, Mass. 02114. Annual Meeting.

American Institute of Ultrasound in Medicine
Secretary, John M. Reid, Ph.D., 556 18th Ave., Seattle, Wash. 98122. Annual Meeting.

American Society of Neuroradiology
Secretary, Dr. David O. Davis, Department of Radiology, 901 Twenty-third St., N. W., Washington, D. C. 20037. Annual Meeting, Boston, Mass., April 26–28, 1973.

Thirteenth International Congress of Radiology
President-Elect, Dr. Juan Gómez López. *Secretary General*, Dr. José Bonmatí, Lagasca, 27 Madrid 1, España. Meeting: Madrid, Spain, Oct. 15–20, 1973.

International Society of Radiology
Hon. Secretary-Treasurer, Prof. Eric Samuel, Radiologist-in-Charge, The Royal Infirmary, Edinburgh EH3 9Y-W, Scotland.

Eleventh Inter-American Congress of Radiology
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colorado 80907. Meeting: Bogotá, Colombia in 1975.

Inter-American College of Radiology
President, Dr. Miguel Dao y Dao, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A.
Secretary General, Dr. Rubén Merenfeld, Instituto Diagnóstico, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A. Meeting: Bogotá, Colombia in 1975.

Third Congress of the European Association of Radiology
Meeting in June, 1975 in Edinburgh, Scotland.

Second Asian and Oceanian Congress of Radiology
Honorary Secretary, Dr. J. J. Martin, Box 805 F., G.P.O., Melbourne, 3001, Australia.
Meeting in 1975.

Alabama Chapter of ACR
Secretary-Treasurer, Dr. Lowry R. Young, Jr., 905 Madison St., Huntsville, Ala. 35801. Meets time and place of Alabama State Medical Association.

Alaska Radiological Society
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

American Thermographic Society
Secretary-Treasurer, Dr. Marc. S. Lapayowker, Department of Radiology, Temple Univ. Hosp., 3401 N. St., Philadelphia, Pa. 19140. Meets at New York-Hilton Hotel, June 23 and 24, 1973.

Arizona Radiological Society, Chapter of ACR
Secretary, Dr. Wesley S. Fee, 2421 E. 6th St., Tucson, Ariz. 85719. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Ark-La-Tex Radiological Society
Secretary, Dr. Erich K. Lang, Confederate Memorial Medical Center, LSU School of Medicine, Shreveport, La. 71101.

Arkansas Chapter of ACR
Secretary-Treasurer, Dr. David H. Newbern, 4301 W. Markham, Little Rock, Ark. 72205. Meets twice annually, the Spring Meeting being in conjunction with and at the place of the State Medical Association.

Association of University Radiologists
Secretary-Treasurer, Dr. Melvyn H. Schreiber, 2909 Dominique Dr., Galveston, Tex. Annual Meeting, Vancouver, B. C., Canada, May 9–12, 1973.

Atlanta Radiological Society
Secretary-Treasurer, Dr. Ernst Ruder, Dept. of Radiol., Crawford Long Memorial Hosp., Atlanta, Ga. 30308. Meets on four Thursday evenings during the academic year at a time announced in early September of each year, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

Bavarian-American Radiologic Society
Secretary, Lucien F. Burke, Maj. MC, Radiol. Service, US Army Gen. Hosp., Frankfurt, APO, New York 09757.

Blockley Radiological Society
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

Bluegrass Radiological Society
Secretary-Treasurer, Dr. Eugene Slusher, Lexington

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Clinic, 1221 S. Broadway, Lexington, Ky. 40504. The Society meets once each month during the school year.

BRONX RADIOLOGICAL SOCIETY, NEW YORK STATE, CHAPTER ACR
Secretary-Treasurer, Dr. Leon J. Corbin, 1369 Rosedale Ave., Bronx, N. Y. 10472. Meets 4 times a year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Sarah Lieberson, 1298 St. Marks Ave., Brooklyn, N. Y. 11213. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Ru-Kan Lin, 191 North St., Buffalo, N. Y. 14201. Meets second Monday evening each month, October to May inclusive, at University Club.

CALIFORNIA RADIATION THERAPY ASSOCIATION
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets semiannually in San Francisco and Los Angeles.

CALIFORNIA RADIOLOGICAL SOCIETY, CALIFORNIA CHAPTER OF ACR
Secretary-Treasurer, Dr. John L. Gwinn, 4650 Sunset Blvd., Los Angeles, Calif. 90027.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P.O. Box 10, Rutherford College, N. C. 28671. Meets every Thursday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:30 P.M.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. John Sanborn, Radiology Department, Crouse-Irving Memorial Hosp., Irving Ave., Syracuse, N. Y. 13210. Meets first Monday each month October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Terry Meyer, 175 S. Merkle Rd., Columbus, Ohio 43209. Meets second Thursday in October, November, January, and March 15, and May 19 at Fort Hayes Hotel, Columbus, Ohio.

CHICAGO RADIOLOGICAL SOCIETY, DIVISION OF THE ILLINOIS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Raymond L. Del Fava, 355 Ridge Ave., Evanston, Ill. 60202. Meets third Thursday of each month, October to April, except December, at the Bismarck Hotel, Chicago, Ill.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Alvin Segel, 3395 Scranton Rd., Cleveland, Ohio 44109. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

COLORADO RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Jerome D. Sutherland, 3705 E. Colfax Ave., Denver, Colo. 80206. Meets third Friday of each month at Denver Athletic Club from September through May.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meets in April and October.

DALLAS-FORT WORTH RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Norman L. Presley, 222 Medical Tower, 1550 W. Rosedale, Fort Worth, Tex. 76104. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Tex.

DELAWARE CHAPTER OF ACR
Secretary, Dr. Seymour R. Kaplan, Kent Gen. Hosp., Dover, Del. 19901.

EAST BAY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Peter E. Kane, Children's Hosp. Med. Ctr., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

EAST TENNESSEE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George H. Wood, 205 Medical Arts Bldg., Knoxville, Tenn. 37902. Meets in January and September.

FLORIDA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Ralph C. Aye, Tampa General Hospital, Tampa, Fla. 33606. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. J. C. Hewitt, 1 Davis Blvd., Tampa, Fla. 33606. Meets in January, March, May, July, September and November.

GEORGIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Richard S. Colvin, Emory University Clinic, Atlanta, Ga. 30322. Meets in spring and fall at Annual State Society Meeting.

GREATER CINCINNATI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

GREATER LOUISVILLE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

GREATER MIAMI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Stanley I. Worton, 1400 N.W. 10th Avenue, Miami, Florida 33136. Meets monthly, third Wednesday at 8:00 P.M. at various member hospitals, Miami, Fla.

GREATER ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary-Treasurer, John J. Lang, 507 Fairways Circle, St. Louis, Mo. 63141.

HAWAII RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Raymond W. Brust, Jr., St. Francis Hosp., 2260 Liliha St., Honolulu, Hawaii 96817. Meets third Monday of each month at 7:30 P.M.

HEALTH PHYSICS SOCIETY
Secretary, John H. Pingel, Argonne National Laboratory, 9700 S. Cass Ave., Argonne, Ill. 60439. Annual Meeting: Deauville Hotel, Miami Beach, Fla., June 17–21, 1973.

HOUSTON RADIOLOGICAL SOCIETY
Secretary, Dr. Neill B. Longley, 6436 Fannin, Suite 601, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

IDAHO STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Hugh P. Smith, Jr., 130 E. Bannock, Boise, Id. 83702. Meets in the spring and fall.

ILLINOIS RADIOLOGICAL SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. B. Jay Hill, Mercy Hospital, Stevenson at King Drive, Chicago, Ill. 60616. Meets in the spring and fall.

INDIANA ROENTGEN SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. L. Ray Stewart, 852 S. Alvord Blvd., Evansville, Ind. 47714.

IOWA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. John Huston Jr., 1948 First Ave. N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ralph H. Baehr, 310 Medical Arts Bldg., Topeka, Kan. 66604. Meets in spring with State Medical Society and in winter on call.

KENTUCKY CHAPTER OF ACR
Secretary-Treasurer, Dr. Joseph G. Whelan, Jr., 1313 St. Antony Place, Louisville, Ky. 40204. Meets in April and September.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N.Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

KNOXVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Jerome Zwanger, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. Gabriel H. Wilson, UCLA Center for Medical Sciences, Los Angeles, Calif. 90024. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif. Midwinter Radiological Conference.

Louisiana Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Robert T. Cook, Southern Baptist Hosp., 2700 Napoleon Ave., New Orleans, La. 70115.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Tex. 77701.

Maine Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Richard W. Taylor, Radiology Department, St. Mary's General Hospital, Lewiston, Maine 04240. Meets in June, September, December and April.

Maryland Radiological Society, Chapter of ACR
Secretary, Dr. George Burke, 4000 North Charles St., Baltimore, Md. 21218.

Massachusetts Radiological Society, Chapter of ACR
Secretary, Dr. Norman L. Sadowsky, The Faulkner Hosp., 1153 Centre St., Jamaica Plain, Mass. 02130.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Jerry C. Phillips, The University of Tennessee College of Medicine, Department of Radiology, Walter C. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday Oct. through May at the University Club.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Ind. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Michigan Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. George A. Kling, Harper Hospital, 3825 Brush St., Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. Thomas C. Lipscomb, 1004 North Tenth St., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Harlan W. Hawkinson, 6 Buffalo Rd., St. Paul, Minn. 55110. Meets twice annually, fall and winter.

Mississippi State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Nancy W. Burrow, 1327 Peachtree St., Jackson, Miss. 39202. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ronald G. Evens, Mallinckrodt Institute of Radiology, 510 S. Kingshighway, St. Louis, Mo. 63110.

Montana Radiological Society, Chapter of ACR
Secretary, Dr. Dexter W. Johnson, Columbus Hosp., Great Falls, Mont. 59401.

Nebraska Chapter of ACR
Secretary-Treasurer, Dr. John T. McGreer, III, 924 Sharp Bldg., Lincoln, Nebr. 68508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society, Chapter of ACR
Secretary, Dr. William G. Arbonies, 887 Marsh, Reno, Nev. 89520.

New England Roentgen Ray Society
Secretary, Dr. Stefan C. Schatzki, 1180 Beacon St. Brookline Mass. 02146. Meets the third Friday of each month, October through April, excluding December, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

New Hampshire Roentgen Ray Society, Chapter of ACR
Secretary-Treasurer, Dr. Edward P. Kane, Claremont Gen. Hosp., Claremont, N. H. 03743. Meets four to six times yearly.

New Mexico Society of Radiologists, Chapter of ACR
Secretary, Dr. Carole R. Simmons, Dept. of Radiol., Presbyterian Hospital Center, Albuquerque, N. M. 87106. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New Orleans Radiological Society, Inc.
Secretary-Treasurer, Dr. Jimmy L. Mains, P.O. Box 446, Gretna, La. 70053. Meets bimonthly at local restaurants selected by the President.

New York Roentgen Society
Secretary-Treasurer, Dr. Howard R. Gould, 153 West 11th Street, New York, N. Y. 10011. Meets monthly on the 3rd Monday at the New York Academy of Medicine at 4:30 P.M. Annual Spring Conference, Waldorf-Astoria Hotel, New York, N. Y., Apr. 26–28, 1973. Further information may be obtained from Dr. Albert A. Dunn, Roosevelt Hosp., New York, N. Y. 10019.

New York State Chapter of ACR
Secretary-Treasurer, Dr. John J. Magovern, 74 N. Village Ave., Rockville Centre, N. Y. 11570.

North Carolina Chapter of ACR
Secretary-Treasurer, Dr. James F. Martin, 300 S. Hawthorne Road, Winston-Salem, N. C. 27103.

North Dakota Radiological Society, Chapter of ACR
Secretary, Dr. Marshall Landa, 1702 13th St., So., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. David F. Bew, University Hospital of Jacksonville, 655 W. Eighth Street, P.O. Box 2751, Jacksonville, Florida 32203. Meets quarterly in March, June, September and December.

Northeastern Oklahoma Radiological Society
Secretary-Treasurer, Dr. Theodore J. Brickner, Jr., 5919 S. Gary Place, Tulsa, Okla. 74110.

Northeastern New York Radiological Society
Secretary, Dr. Robert C. Friedman, 325 Presidential Way, Guilderland, N. Y. 12085. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiation Therapy Association
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets quarterly.

Northern California Radiological Society
Secretary, Dr. J. Richard McProuty, 6620 Coyle Ave., Carmichael, Calif. 95608. Meets fourth Monday of Nov., Jan., and March at the Mansion Inn, Sacramento, Calif.

Northwestern New York Radiological Society
Secretary, Dr. Barbara E. Chick, Glens Falls Hospital, Glens Falls, N. Y. 12801.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society, Chapter of ACR
Secretary, Dr. Thomas F. Ulrich, Barberton Citizens Hospital, Barberton, Ohio 44203.

Oklahoma State Radiological Society, Chapter of ACR
Secretary, Dr. George H. Ladd, 4616 Denison, Muskogee, Okla. 74401. Meets in January, May and October.

ORANGE COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Norman Arnett, 400 North Pomona, Fullerton, Calif. 92632. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

OREGON STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ronald W. Philips, 2305 Washington, Milwaukie, Ore. 97222. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Oregon 97005. Annual meeting: Benson Hotel, Portland, Ore., May 11–13, 1973.

PENNSYLVANIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Theodore A. Tristan, Harrisburg Polyclinic Hosp., Harrisburg, Pa. 17105.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Howard M. Pollack, Department of Radiology, Episcopal Hospital, Philadelphia, Pa. 19125. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Stephen C. Bruno, Shadyside Hospital, 5230 Centre Ave., Pittsburgh, Pa. 15232. Meets second Wednesday of month, September through May, at the Pittsburgh Athletic Association.

RADIATION RESEARCH SOCIETY
Executive Secretary, Richard J. Burk, Jr., 4211 39th St., N.W., Washington, D. C. 20016. Annual Meeting: St. Louis, Mo., April 29–May 3, 1973. International Congress of Radiation Research, Seattle, Wash., July 14–20, 1974.

RADIOLOGICAL SOCIETY OF CONNECTICUT, INC., CHAPTER OF ACR
Secretary-Treasurer, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meetings are held quarterly.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary-Treasurer, Dr. Alvin Nathan, c/o Academy of Medicine, 320 Broadway, Cincinnati, Ohio 45202. Meets first Monday of each month at Cincinnati Academy of Medicine.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
President-Secretary, Dr. Arch W. Templeton, Univ. of Kansas Med. Ctr., Kansas City, Kansas 66103. Meets 5 times a year on given dates.

RADIOLOGICAL SOCIETY OF LOUISIANA, CHAPTER OF ACR
Secretary-Treasurer, Dr. Robert T. Cook, 1820 Octavia St., New Orleans, La. 70115. Meets semiannually during Louisiana State Medical Society meeting and 6 months later.

RADIOLOGICAL SOCIETY OF NEW JERSEY, CHAPTER OF ACR
Secretary, Dr. Sidney Ketyer, St. Elizabeth Hosp., 225 Williamson St., Elizabeth, N. J. 07207. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

RADIOLOGICAL SOCIETY OF RHODE ISLAND, CHAPTER OF ACR
Secretary-Treasurer, Dr. Daniel J. Hanson, 116 Nayatt Rd., West Barrington, R. I. 02806.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary-Treasurer, Dr. Marshall Rowen, Dept. Radiol., St. Joseph Hosp., 1100 Stewart Dr., Orange, Calif. 92668. Meets three times a year, usually October, February and May.

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Donald P. King, 218 Gun Club Rd., Richmond, Va. 23221. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary-Treasurer, Dr. Kenneth E. Robinson, 1441 East Avenue, Rochester, New York 14610. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Lorenz R. Wurtzebach, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 2–4, 1973.

SAN ANTONIO-CIVILIAN MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Robert M. Maurer, Santa Rosa Medical Center, San Antonio, Tex. 78207. Meets third Wednesday of each month at Fort Sam Houston Officers' Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY
President, James R. Collins, 340 Fourth Ave. Suite 15, Chula Vista, Calif. 92010. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. James G. Moore. Mary's Help Hospital, 1900 Sullivan Ave., Daly City, Calif. 94015.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

SECTION ON RADIOLOGY, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

SECTION ON RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Mario A. Calonje, 1514 Jefferson Highway, New Orleans, La. 70121. Annual Meeting.

SECTION ON RADIOLOGY, TEXAS MEDICAL ASSOCIATION
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027. Annual meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 23–24, 1973.

SOCIETY OF GASTROINTESTINAL RADIOLOGISTS
Secretary-Treasurer, Dr. Wm. B. Seaman, The Presbyterian Hospital, Columbia-Presbyterian Medical Center, 622 W. 168th St., New York, N. Y. 10032.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Dr. E. James Potchen, Edward Mallinckrodt Institute of Radiology, 660 S. Euclid Ave., St. Louis, Mo. 63110. *Administrative Officer*, Mrs. Margaret Glos, 211 E. 43rd St., New York, N. Y. 10017. Annual meeting: Americana Hotel, Miami Beach, Fla., June 12–15, 1973.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. A. D. Benjamin, 596 Carroll St., Sunnyvale, Calif. 94086. Meets the 2nd Monday of each month at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

SOUTH CAROLINA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTH COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. James T. McClintock, P.O. Box 837, Santa Barbara, Calif. 93102. Meets fourth Monday of the month, Oct. through May.

South Dakota Radiological Society, Chapter of ACR
Secretary, Dr. M. F. Petereit, 2416 S. Phillips, Sioux Falls, S. D. 57105. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. John Byfield, 1000 West Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 7544, Mobile, Ala. 36607.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Carl T. Stubblefield, Bedford County Hospital, Columbia, Tenn. 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas State Radiological Society, Chapter of ACR
Secretary, Dr. Herman C. Sehested, 815 Medical Tower, Room 100, 1550 W. Rosedale St., Fort Worth, Tex. 76104. Annual meeting.

The Fleischner Society
President, Dr. Robert G. Fraser, 1555 Summerhill Ave., Montreal 109, P.Q., Canada. Annual meeting.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John F. Stucki, Department of Radiology, McKay-Dee Hosp., 3939 Harrison Blvd., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society, Chapter of ACR
Secretary, Dr. J. Lorimer Holm, R.R.#3, Barre, Vt. 05641.

Virginia Chapter of ACR
Secretary-Treasurer, Dr. James S. Redmond, Suite 7, Medical Center, Lynchburg, Va. 24501. Next Meeting: Nov. 6, 1972 at the Conference Ctr., Williamsburg, Va.

Washington, D. C., Chapter of ACR
Secretary-Treasurer, Dr. Albert M. Zelna, 9110 Seven Locks Rd., Bethesda, Md. 20014.

Washington State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John N. Roehr, 1011 Medical Dental Bldg., Seattle, Wash. 98101.

West Virginia Radiological Society. Chapter of ACR
Secretary-Treasurer, Dr. Andrew W. Goodwin, II, 200 Med. Arts Bldg., Charleston, W. Va. 25301. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Max C. King, 314 Woodland Hills Rd., White Plains, N. Y. 10603. Meets on second Tuesday of October, December, February and May.

Wisconsin Radiological Society. Chapter of ACR
Secretary-Treasurer. Dr. Marvin L. Hinke, 630 S. Central Ave., Marshfield, Wisc. 54449. Meets twice a year, May and September.

Wisconsin Society of Therapeutic Radiologists
Secretary. Dr. Robert W. Edland, Gundersen Clinic, LaCrosse, Wisc. 54601. Meets quarterly.

Wyoming Radiological Society, Chapter of ACR
Secretary, Dr. Ross J. Collie, Box 96, Lander, Wyo. 82520. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costarricense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá
Secretary-General, Dr. Francisco Mirambell, Apartado 3352, San José, Costa Rica, Central America.
Meets annually in a rotating manner in the six countries.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad de Radiología de El Salvador
Secretary, Dr. Carlos Mejia, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D.F., México.
Secretary-General, Dr. Jorge Cano Coquí. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Heriberto Pagán Sáez, Box 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Moyne, 121 Boul. Taschereau, Greenfield Park, P.Q., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. T. Kerr, 32 Welbeck St., London, W1M/7PG, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics
Honorary Secretary-Treasurer, Dr. R. G. Baker, Ontario Cancer Foundation, Ottawa Civic Clinic, 1053 Carling Ave., Ottawa 3, Ont., Canada.

Canadian Association of Radiologists
Honorary Secretary, Dr. Champlain Charest, 1555 Summerhill Ave., Montreal 109, Que., Canada. Annual meeting: Montreal, Que., Canada, March 11–17, 1973.

Edmonton and District Radiological Society
Secretary, Dr. L. A. Koller, Suite 360, Professional Bldg., 10830 Jasper Ave., Edmonton 15, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Robert Morrison, 47 Lincoln's Inn Fields, London, W.C.2, England. The scientific meetings held in January, February and March 1973 will be combined sessions with the British Institute of Radiology and the Section of Radiology of The Royal Society of Medicine.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Hon. Secretary, Dr. D. F. Canwell, 123 St. Stephens Green, Dublin 2, Ireland.

Montreal Radiological Study Club
Secretary, Dr. W. Paul Butt, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 8:15 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1 M&AE, 1 England.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Hubert Sasseville, Verdun Hospital, Montréal, P.Q., Canada. Meets every third Tuesday from October to April.

The Hospital Physicists' Association
Honorary Secretary, J. B. Massey, B.Sc., Christie Hosp. and Holt Radium Institute, Physics Department, Withington, Manchester M20 9BX, England.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

Royal College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, 147 Macquarie St., Sydney, N.S.W. 2000, Australia.

South America

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Federación Argentina de Sociedades de Radiología
Branches of the Federation are: Sociedad de Radiólogos de la Provincia de Córdoba; Sociedad Argentina de Radiología; Asociación Argentina de Radiología; Sociedad de Radiología, Radioterapéutica y Medicina Nuclear de Rosario; Sociedad de Radiología y Medicina Nuclear del Centro y Sudeste de la Provincia de Buenos Aires (Mar del Plata); Sociedad Salteña de Radiología y Medicina Nuclear; Sociedad de Radiología de Tucumán; Sociedad de Radiologia del Nordeste Argentino; Sociedad de Radiología de La Plata; and Sociedad de Radiología de San Juan.
Secretary-General-Treasurer, Dr. Roberto Habichayn, Av. Colón 637, Córdoba, Argentina.

Sociedad Argentina de Radiología
Secretary-General, Dr. Armando B. de Onaindia, Santa Fé 1171, Buenos Aires, Argentina. Meets first Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Caixa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Claudio Cortés, Casilla, 13426 Santiago, Chile. Meets first Friday of each month at Av. Santa María 1810 at 7:00 P.M.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Rodrigo Caro Molina, Cali, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología
Secretary, Dr. Carlos Palau Jimenez, Casilla 5469, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Hugo Volpe Rios, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dr. Miguel Chiappori Cambana, Av. General Santa Cruz No. 315, Miraflores, Lima, Perú, Casilla Correo, 2306, Lima, Perú. Meets monthly except during January, February, and March.

Sociedad de Radiología del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología del Nordeste Argentino
Secretary-General, Dr. Francisco J. Velar, Catamarca 561, Corrientes, Argentina.

Sociedad de Radiología de La Plata
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Sociedad de Radiología, Cancerología y Física Médica del Uruguay
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Sociedade de Radiología de Pernambuco
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Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad de Radiología, Radioterapéutica y Medicina Nuclear, de Rosario
Secretary-General, Dr. Federico Frágola, Santa Fe 1798, Rosario, Argentina.

Sociedad Salteña de Radiología y Medicina Nuclear
Secretary, Dr. Julio Luis Baldi, Av. Sarmiento 536, Salta, Argentina.

Sociedad Venezolana de Radiología y Medicina Nuclear
Secretary-General, Dr. Salvador Itriago Borgas, Apartado Postal 9213, Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
Secretary, Dr. Ernst Kotcher, Wiener Allgemeine Poliklinik Mariannengasse 10, A-1090 Wien, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. The 1973 Annual Meeting is a joint meeting with the Deutsche Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Secretary, Dr. P. Hicken, The Children's Hosp., Ladywood Middleway, Birmingham B16 8ET, Great Britain. Tenth Annual Meeting, Birmingham, April 11–13, 1973.
Permanent Secretary, Clément Fauré, Hôpital des Enfants-Malades, 149, rue de Sèvres, 75 Paris 15e, France.

Société Française de Radiologie Médicale, Médecine Nucléaire et Electrologie, and its branches: Société du Sud-Ouest, du Littoral méditerranéen, du Centre et Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et du Massif Central. Parent Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Société Française de Neuroradiologie
Secretary-General, Professeur agr. R. Djindjian 16, rue de l'Université 75, Paris 7e, France. Annual meeting.

Československá Radiologická Společnost
Secretary, Associate Professor Jaromír Kolář, M.D., Sc.D., Radiological Clinic, Praha 2, U nemocnice 2, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Walter Frommhold, Director of Medizinisches Strahleninstitut der Universität Tübingen, Röntgenweg 11, 7400 Tübingen, Germany.

The 1973 Annual Meeting is a joint meeting with the Österreichische Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Società Italiana di Radiologia Medica e Medicina Nucleare
Administrative Secretary, Prof. E. Conte, Ospedale Mauriziano, 10128 Torino, Italy. Meets annually.

Societas Radiologica Danica
Secretary, Dr. Bent Langefeldt, Tretommervej 20a, DK-8240 Risskov, Denmark.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. J. D. Mulder, Dept. of Rad., Akademisch Ziekenhuis, Leiden, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Dr. José Bonmatí, Villanueva, 11, Madrid 1, España. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Sociedade Portuguesa de Radiologia e Medicina Nuclear
Secretary-General, Dr. Luís Aires de Sousa, Av. Elias Garcia, 123- 1, Esg.-Lisboa i-Portugal.

Schweizerische Vereiningung für Radiologie, Nuklearmedizin und Strahlenbiologie (Association Suisse de Radiologie, Médecine Nucléaire et de Radiobiologie)
Secretary, Dr. med. Gustav Schoch, Bethesdaspital, Gellerstrasse 144, 4000 Basel, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. L. R. Parthasarathy, 44 Constable Road, Madras—23, India.

Indonesian Radiological Society
Secretary, Dr. Gani Iljas Sasmitaatmadja, Radiology Dep., Faculty of Medicine, University of Indonesia, Salemba 6, Djakarta, Indonesia.

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month. Third National Iranian Congress of Radiology: Isfahan, Iran, May 5–10, 1973. Deadline for acceptance of papers Feb. 20, 1973.

Israel Radiological Society
President, Dr. I. Izkovitch, 2 Wingate Ave., Beit Harofe, Haifa, Israel.

Japanese American Radiological Society
Secretary, Thomas J. Imray, Maj. MC, Chief, Radiol. Dep., US Army Hosp., Camp Zama, Japan, APO San Francisco, Calif. 96343. Meets 3rd Thursday, monthly at various locations in Tokyo.

Philippine College of Radiology
Secretary-Treasurer, Dr. Edmundo V. Villacorta, Box 1284, Commercial Center, Makati, Rizal D-708, Philippines. Meets every 3 weeks on Fridays. Annual convention.

Radiological Society of Thailand
Secretary, Prof. Rojana Suvansuthi, M.D., Ph.D., Depart. of Rad., Sirizaj Hospital, Faculty of Medicine, Mahidol University, Bangkok 7, Thailand.

Africa

Association of Radiologists of West Africa
Honorary Secretary, Dr. T. M. Kolawole, University College Hospital, University of Ibadan, Ibadan, Nigeria.

Radiological Society of South Africa
Secretary, Dr. B. Rosenberg, P.O. Box 3200, Johannesburg, South Africa.

South African International Radiological Congress
Director, Dr. Paul Sneider, P.O. Box 4878, Johannesburg, South Africa.

ABSTRACTS OF RADIOLOGIC LITERATURE

E. FREDERICK LANG, M.D., Editor

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ROENTGEN DIAGNOSIS

Head

Grunert, V., Mostbeck, A., and Valencak, E. Messung pathologischer AV-Kurzschlüsse im Gehirn. (Measurement of pathologic arteriovenous shunts in the brain.) *Wien. klin. Wchnschr.*, Aug., 1972, *84*, 530–533. (Address: Dr. V. Grunert, Neurochirurgische Universitätsklinik, Alser Strasse 4, A-1090 Wien, Austria.)

Intraarterially injected I^{131} labeled albumin particles (diameter 5 to 50 μ) remain in the capillaries of the corresponding artery. A–V malformations have a larger diameter than the capillaries and a certain proportion of the particles are immediately shunted into the venous circulation and trapped in the capillary bed of the lungs.

The shunt volume is proportional to the increase of radioactivity in the lungs. Intravenous injection of particles allows calculation of the shunt volume. Two cases of carotid-cavernous fistula were found to have shunt volumes of 76 and 90 per cent, respectively. In 9 cases of intracerebral A–V malformation the measured shunt volumes ranged from 60 to 94 per cent. The shunt volumes fell to 10–15 per cent postoperatively.

Scintigrams obtained after the intraarterial injection of particles revealed diminished or absent trapping of particles over the A–V malformation with additional hemodynamic changes distally. Postoperative scintigrams showed normalization of the vascular distribution.—*Peter F. Winter, M.D.*

Campbell, A. J., and Bull, J. W. D. Craniopharyngioma in a predominantly adult population: a radiologic review. *J. Canad. A. Radiologists*, Sept., 1972, *23*, 182–191. (Address: A. J. Campbell, M.D., Department of Diagnostic Radiology, Victoria General Hospital, Halifax, Nova Scotia, Canada.)

The authors have extensively reviewed the clinical and radiologic findings of 26 cases of craniopharyngioma seen in an 11 year period at the National Hospital, Queen's Square, London, England. The purpose was to compare the differences in symptomatology, clinical and radiographic findings with those reported in the literature and to assess the value of brain scanning in diagnosis.

The present cases included 17 females and 9 males with the youngest 8 years of age and the oldest 65 years.

All cases were verified by craniotomy and/or autopsy. All the adult patients presented at the time of admission with some visual disturbance such as blurring of vision, loss of temporal vision, diplopia or light flashes, and in 14 patients, the first symptoms were visual. Headache was the initial symptom in 6 patients and present in 14. No specific headache pattern could be identified. Six patients presented with pituitary-hypothalamic dysfunction and this complex was present in 16 patients. Varying degrees of mental deterioration were seen in 6 patients. No case of increased intracranial pressure was seen over the age of 30 years.

Plain film roentgenographic studies were normal in 10 cases and questionable in 2.

Several types of sellar alterations are described. Twenty per cent of the adult cases had flocculent calcifications. Two of 7 isotope scans were positive and in both, technetium 99m was utilized. Six of 20 angiographic examinations were considered positive and all vertebral angiograms were negative. Each patient had pneumoencephalography, ventriculography or both examinations. Characteristic pneumographic findings were obliteration of the recesses at the anterior end of the third ventricle, well-defined filling defects causing displacement of the anterior extremity of the third ventricle, encroachment on the chiasmatic interpeduncular or pontine cisterns by a soft tissue mass or upward displacement of the anterior horns of the lateral ventricles.

Twenty-two tumors were cystic or cystic with solid components, and 2 were solid.

Eight patients showed a satisfactory response to therapy.

The latter half of the paper reviews the etiology, pathology, symptomatology and radiographic findings as reported in the literature. Sixteen differential diagnoses are discussed.—*John T. Underberg, M.D.*

Pochaczevsky, Rubem, Sussman, Richard, and Stoopack, Jerome. Arteriovenous fistulas of the maxillofacial region. *J. Canad. A. Radiologists*, Sept., 1972, *23*, 201–206. (From: Departments of Radiology and Dental and Oral Surgery, the Jewish Hospital and Medical Center of Brooklyn, Greenpoint Hospital Affiliation and the Department of Radiology of the State University of New York, Downstate Medical Center, Brooklyn, N. Y.)

The authors briefly summarize the etiology and clinical findings of arteriovenous fistulas of the maxillofacial region and contribute 5 case reports with adequate angiographic studies.

Arteriovenous fistulas of the maxillofacial region may be congenital or acquired. Congenital malformations are divided into capillary and cavernous hemangiomas. Appreciation of the existence of congenital arteriovenous fistulas and their extent with involvement of root sockets is important prior to dental extraction, as 2 of the 5 cases summarized involved adults who suffered severe hemorrhage following dental extraction. These lesions otherwise are generally brought to a physician's attention because of cosmetic reasons.

Acquired arteriovenous fistulas are usually secondary to a penetrating facial wound and are often symptomatic. Development of a mass associated with buzzing, thrill or bruit is the common finding.

Plain film roentgenographic studies, in the case of congenital malformations, may reveal numerous phleboliths. Both congenital and acquired fistulas can be demonstrated and their extent defined by arteriography. The presence of malignancy and a rapidly enlarging mass can be excluded and a better surgical approach, when indicated, can be defined.

The authors suggest that embolization techniques may be utilized in the future for treatment of these lesions.—*John T. Underberg, M.D.*

NECK AND CHEST

STANCIU, C., and BENNETT, JOHN R. Smoking and gastro-oesophageal reflux. *Brit. M. J.*, Sept., 1972, *3*, 793–795. (From: Gastrointestinal Unit, Royal Infirmary, Hull, England.)

Twenty-five habitual smokers, aged 24 through 71 years, all of whom had heartburn related to position and meals, were studied for acid gastroesophageal reflux and esophageal pressure changes related to smoking. Fourteen had roentgenographically documented gastroesophageal reflux.

Two polyethylene catheters, each containing a combined glass-reference pH electrode, were connected to a multichannel direct writing recorder via pressure transducers and positioned in the distal esophagus for studies carried out under control conditions to determine gastroesophageal sphincter pressure and acid gastroesophageal reflux as influenced by smoking and provocative maneuvers to elicit the possible reflux.

During smoking there was a significant drop in gastroesophageal sphincter pressure and the number of maneuvers eliciting reflux increased. It is postulated that the inhaled nicotine causes relaxation of the circular musculature of the distal esophagus. Reflux may occur without symptoms, but heartburn may be a product of repeated reflux aggravated by smoking, and cigarette smoking should be a reversible aggravating cause of gastroesophageal reflux.—*John T. Underberg, M.D.*

KEIGHLEY, M. R. B., GIRDWOOD, R. W., IONESCU, M. I., and WOOLER, G. H. Spontaneous rupture of the oesophagus: avoidance of postoperative morbidity. *Brit. J. Surg.*, Aug., 1972, *59*, 649–652. (Address: M. R. B. Keighley, Surgical Registrar, Leeds [St. James's] University Hospital, Leeds LS9 7TF, England.)

Twelve cases of spontaneous rupture of the esophagus are summarized.

Seventy-five per cent of these patients were men and the average age was 57 years. With 1 exception all the patients presented with severe chest pain and dyspnea. Seven patients complained of severe abdominal pain with clinical signs of upper abdominal peritonitis and 4 patients had shoulder pain. Subcutaneous emphysema of the neck was present in 58 per cent. There was only 1 case in whom a chest roentgenogram did not confirm the presence of air or fluid in the affected pleural cavity. Mediastinal emphysema was seen in 3 patients and only 1 patient had roentgenographic evidence of air in the peritoneal cavity.

A gastrographin swallow performed in 8 patients was without exception both diagnostic of esophageal perforation and provided evidence of the site and extent of the leakage.

The results of esophagoscopy as a diagnostic measure were less reliable, with evidence of rupture in only 4 of the 6 patients in whom this was performed preoperatively.

The site of rupture was recorded within the lower third of the esophagus in all except 1 patient.

Operative records described the tear as being longitudinal in direction, posterolateral in position, and predominantly on the left side. Direct suture of the perforation was undertaken in every case. Feeding jejunostomy was also undertaken as a primary or secondary procedure in 5 patients. There was only 1 death in this series (an incidence of 8 per cent); this occurred in a patient who was admitted moribund with a tension pyopneumothorax.

The incidence of postoperative complications was considerable, occurring in 10 of the 11 survivors. These complications were largely the result of further leakage from the site of perforation, resulting in the formation of empyemata, esophagopleural fistulae, a mediastinal abscess and a persistent sinus in the wound. Evidence of leakage or stricture formation at the suture line was shown on postoperative contrast roentgenography in half of the cases. Subphrenic abscess formation was demonstrated in 2 patients.

Most cases of spontaneous rupture occurred following forceful vomiting and particularly after attempts had been made to suppress this desire by contraction of the cricopharyngeus.

The importance of prompt diagnosis and surgical repair is stressed. The value of contrast esophagography for diagnostic purposes as well as for detection of persistent postoperative leakage is emphasized.—*David Morse, M.D.*

HÜGEL, E., LANGE, P., DIERKESMANN, R., and MARTIN, H. Pneumocystis-Pneumonie des Erwachsenen. (Pneumocystis pneumonia in adults.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Aug., 1972, *117*, 151–161. (Address: Dr. E. Hügel, 6

Frankfurt 70, Theodor-Stern-Kai 7, Germany.)

Pneumocystis carinii infestation in adults is the result of an impaired defense mechanism due either to serious disease or to treatment with corticosteroids, or cytostatic or immunosuppressive drugs.

The authors observed a patient with chronic myelogenous leukemia, who passed through various stages of this complication while undergoing treatment. The patient's roentgenographic appearance of *Pneumocystis carinii* infestation was variable. At the beginning, multiple ill-defined, streaky and patchy densities with irregular distribution were found, which disappeared after institution of corticosteroid therapy. The first recurrence, which occurred after a reduction of the corticosteroid dose, showed again focal infiltrates, but with increased density and spread to the upper lung fields. The pulmonary findings improved promptly after increase of the corticosteroid dose. The terminal phase showed a homogeneous, diffuse density in both lungs.

The results of experimental *Pneumocystis carinii* infestation in animals were used to interpret this course of human infestation. Rats with maximum reduction of resistance due to high dose application of corticosteroids were found to have an abundance of *Pneumocystis carinii* organisms in the lungs, but the interstitial reaction was minimal, if not absent. On the contrary, marked interstitial reaction was found in animals with slight reduction of resistance because of short and low dose or after discontinuation of corticosteroids. These findings explain well the patient's course. The roentgenographic manifestations, which reflect mainly the interstitial reaction, improved after commencement of corticosteroid therapy. It recurred following reduction of the maintenance dose, but improved again after increase of corticosteroids.

The importance of KBR, transtracheal and lung biopsy for the diagnosis is stressed.

The differential diagnosis should include interstitial fibrosis due to bulsulfan or methotrexate therapy as well as pulmonary fungal infection.

The possible treatment of *Pneumocystis carinii* infestation is discussed.—*Peter F. Winter, M.D.*

Abdomen

Oi, M. Itaru. Duodenoscopy during pancreatic diseases. *Arch. franç. d. mal. d. l'appareil digestif*, April–May, 1972, *61*, 349–354. (From: Institute of Gastroenterology, Tokyo Women's Medical College, Tokyo, Japan.)

Tumors of the duodenal papilla, pancreas and biliary duct are frequently diagnosed by duodenoscopy as papillary tumor or rigid, eroded mucosa of the duodenum. Three hundred and ten cases were examined since 1969, and 250 pancreatograms and 134 cholangiograms (pancreatocholangiogram in 117 of them) were obtained without severe complication.

The pancreatic tumor is diagnosed by the obstruction and stenosis of the pancreatic duct in most cases. Tumor outside of the pancreas is also suspected by the compression of the duct. The pancreatic cyst and severe chronic pancreatitis are also diagnosed by obstruction, stenosis and dilatation with irregular branches in pancreatography.

In tumors of the body of the pancreas and of the common hepatic duct, there was no abnormal finding on duodenoscopy in most cases.

When the tumor of the pancreas and the biliary system is large in size and is located near the duodenum, some abnormalities in duodenoscopy, as indirect signs for the existence of tumor, are noted.

The other important diagnostic approach for the pancreatic and biliary diseases by duodenoscopy is cannulation of the duodenal papilla, in order to visualize the pancreatic and biliary ducts, and to obtain the pure pancreatic juice or bile for biochemical analysis, cytology and bacteriologic examination.

The radiocontrast material, urografin 60%, is injected through the cannulated catheter into the pancreatic or biliary ducts under fluoroscopic control, with an image intensifier.

The catheter is usually inserted into the pancreatic duct first, but the insertion is confirmed only by fluoroscopy, injecting a small amount of the contrast medium. The main pancreatic duct and its branches in routine examination are visualized by injecting only 2–4 ml. of opaque medium in order not to damage the pancreas by an excessive amount. The examination is finished within 15 minutes.

The 60 nonvisualized cases were: 4 cases of unsuccessful insertion of the fiber-duodenoscope into the duodenum (including an advanced cancer of the pancreatic head and severe deformity of the thorax); 18 cases of unsuccessful observation of the duodenal papilla; 26 of unsuccessful cannulation; and 12 of nonopacification of ducts after successful cannulation.

The complications directly attributed to this procedure were: submucosal cyst formation of the duodenum; rupture of the main pancreatic duct; temporary depression of the blood pressure; bleeding from the duodenal papilla; and transient elevation of serum amylase and abdominal fullness.

In the case of a tumor of the pancreas and surrounding organs, which were all malignant except for 1 benign retroperitoneal cyst, the pancreatic duct was visualized in 30 out of 50 cases.—*Stephen N. Tager, M.D.*

Rosewarne, M. D. Cystic dilatation of the intrahepatic bile ducts. *Brit. J. Radiol.*, Nov., 1972, *45*, 825–827. (Address: Department of Radiology, Northern General Hospital, Sheffield, England.)

Cystic dilatation of the intrahepatic biliary tree

was described in 1958. The intrahepatic ducts are saccular, contain bile, and communicate freely with each other and with the common bile duct. Biliary calculi and cholangitis are frequently the presenting features. A review of the world literature disclosed that death in all recorded cases was due to liver abscesses and septicemia.

The author describes 2 cases, females, 21 and 51 years old, respectively. One died of unremitting sepsis following a clinical diagnosis of liver abscess, and the other had proved liver abscesses at the time of autopsy.

The classification of congenital cystic disease of the liver is not entirely agreed upon. Some authors feel that it is related to congenital hepatic fibrosis, while others believe that this and congenital cystic disease are separate. Congenital anomalies of the biliary tract may be associated with cystic disease of the kidneys, and the younger of the 2 patients presented with renal tubular ectasia. Cystic dilatation of the intrahepatic bile ducts is apparently separate from the cysts which occur in connection with polycystic disease of the kidneys. The liver cysts in the latter do not communicate with the biliary tree.

The preoperative diagnosis of cystic dilatation of the intrahepatic ducts is difficult, as the extensive changes are not usually appreciated without direct cholangiography.—*E. Frederick Lang, M.D.*

Genitourinary System

Hatfield, Philip M., and Pfister, Richard C. Adult polycystic disease of the kidneys (Potter Type 3). *J.A.M.A.*, Dec., 1972, *222*, 1527–1531. (From: Departments of Radiology [Genitourinary Section], Harvard Medical School, and Massachusetts General Hospital, Boston, Mass.)

Differentiation of adult polycystic kidneys with normal renal function and kidneys with multiple, simple retention cysts is difficult or impossible using clinical, roentgenographic, or routine pathologic methods. Microdissection will permit differentiation. One practical method of making the diagnosis of polycystic disease is demonstrating the coexistence of extrarenal cysts in the liver or pancreas. It has been estimated that 75 per cent of patients with adult polycystic disease remain undetected.

Among 399 patients with pathologically proved multiple cysts in both kidneys, the authors have investigated 58, in whom there were associated cysts in the liver or pancreas, to establish the diagnosis of adult polycystic kidney disease. The authors felt that this did not exclude the strong possibility that numerous others of the 399 patients were actually instances of adult polycystic disease.

The 58 patients fell naturally into 2 groups: the symptomatic, numbering 26; and the 32 asymptomatic patients. Of the symptomatic group approximately one-third presented with a family history of polycystic disease; 23 died at an average age of 52 years; their kidneys weighed twice as much as those of the asymptomatic patients; and their cysts were larger. Of the asymptomatic group only 1 related a family history of polycystic disease, and the average age at death was 73 years. It is not clear whether these differences indicate 2 separate diseases or not. Microdissections have demonstrated no clear cut anatomic differences between the kidneys of 2 symptomatic and 2 asymptomatic adults.

Of the symptomatic patients 12 had renal insufficiency, 7 had hypertension, and 7 had an intracranial aneurysm.

The authors emphasize the difficulty in identifying bilateral polycystic disease with conventional urography. In one-third of the abnormal urograms there were shown only unilateral abnormalities, and all of these were later demonstrated at autopsy to have bilateral multiple cysts. Three of 11 retrograde pyelograms were diagnostic. All infusion nephrotomograms were diagnostic.

Because of the difficulties in both identification and evaluation of these patients, the authors suggest infusion nephrotomography in all patients who demonstrate a unilateral cystic kidney, in the young patient with a ruptured intracranial aneurysm, and in any patient in whom polycystic disease is suspected, even in the presence of a normal or equivocal conventional urogram. Since 32 of the 58 patients were entirely asymptomatic, the usual grave prognosis should be reserved for those with hypertension associated with either intracranial aneurysm or azotemia, and for those in whom the cysts are 3 cm. in diameter or larger.—*E. Frederick Lang, M.D.*

Soloway, Mark S., Hyers, George H., Jr., Johnston, Gerald, and Ketcham, Alfred S. Renography in the evaluation of patients with ileal conduits. *Surg., Gynec. & Obst.*, Oct., 1972, *135*, 521–524. (From: Surgery Branch, National Cancer Institute, and the Department of Nuclear Medicine, Clinical Center, National Institutes of Health, Bethesda, Md.)

Permanent ileal conduit urinary diversion procedures now offer a chance for long survival provided these patients can be protected from the hazards of calculus formation, pyelonephritis, ureteral stricture and upper urinary tract obstruction by early diagnosis. Traditionally, this has been done by semiannual or annual excretory urograms, the repetitive use of which carries with it the inherent risks associated with cumulative radiation as well as idiosyncratic or allergic reaction. This study was designed to evaluate if the radioisotope renogram was as reliable as the excretory urogram in detecting urinary tract obstruction in patients with ileal conduit diversion.

Thirty patients were evaluated by means of reno-

grams and scintiphotos obtained with the use of a scintillation camera, and within 10 days, by excretory urography. The isotope studies were found to be more accurate in the upright position, and following an intravenous injection of 200 μc of iodohippurate sodium I131, the renogram and 2 min. sequential scintiphotos were obtained concomitantly to give a visual record of the passage of the hippuran through the kidneys and upper part of the urinary tracts.

The quantitative evaluation of the renogram for this study was restricted to the time from injection of hippuran to the point of maximum count rate obtained over the kidneys. This time reflects the accumulation of the tracer in the kidney and its excretion from the renal pelvis; in this study it was found to be in the range of from 1 to 5 minutes with normal excretory urograms. For those with minimal degrees of caliectasis and/or pyelectasis there was considerable overlapping of the renographic curves with those without any evidence of dilatation. For those patients judged to have moderate to marked dilatation of the collecting systems, the accumulation times of the isotope within the kidneys were considerably prolonged, usually beyond the 6 minute interval so that there was no overlap with the normal patients.

It was concluded that since an excellent correlation had been demonstrated between the renogram obtained in the sitting position and the excretory urogram, once the urinary tract has stabilized, patients with an ileal conduit may be followed adequately by periodic renograms and plain roentgenograms, in addition to routine laboratory checks of renal function. Significant changes in any of the parameters should then be investigated with excretory urography.—*Donald M. Monson, M.D.*

Hör, G., Pabst, H. W., Pfeifer, K. H., Heidenreich, P., Langhammer, H., and Heinze, H. G. Radionuclides in renal transplantation. *J. Nuclear Med.*, Nov., 1972, *13*, 795–800. (Address: G. Hör, Nuklearmed. Klin. d. TU, Ismaningerstrasse, 8 München 80, Germany.)

Several radionuclides were used to evaluate function and morphologic disorders of renal transplants. I^{131}-o-hippuric acid (IOH) was used for isotope renography and to estimate glomerular and tubular function. IOH measures effective renal plasma flow. In^{113m}, Tc^{99m}, and Yb^{169}-EDTA and DTPA were used for renography and to study glomerular function and renal clearance. Hg^{203}-mersalyl, Hg^{197}-chlormerodrin and I^{131}-fibrinogen have been used for renal scanning and localization. Xe^{133} clearance was used to study extracorporeal cadaver kidney transplants. The renal cortical blood flow was determined by externally monitoring the Xe^{133} washout from the exteriorized kidneys. $Tc^{99m}O_4^-$ was used to study renal vascular perfusion.

Renal clearance studies were done by using I^{131}-o-hippuric acid and Yb^{169}-EDTA for a combined study of renal plasma flow and glomerular filtration. Renal clearance was determined according to the whole body principle.

The following criteria were found in acute rejection crises: (1) IOH accumulation (lack of excretory segments or prolonged secretory maximum), lack of bladder activity and marginal filling defects in the scan; (2) positive correlation between serum creatinine and the elimination index of the IOH and In^{113m}-Fe-EDTA renograms and a negative correlation between serum creatinine and accumulation index of renography; (3) tubular and glomerular function was different in acute tubular necrosis of transplanted cadaver kidneys that were subjected to prolonged ischemia time before transplantation; IOH accumulated without excretion, whereas there was excellent excretion of the In^{113m}-Fe-EDTA; (4) the delayed transit time of IOH in acute tubular necrosis seems to depend on the duration of ischemia time of the cadaver kidney before transplantation; (5) arterial thrombosis or complete occlusion results in total loss of accumulation of radioactivity; (6) rectilinear scans using Hg^{203} or Hg^{197} were characterized by filling defects in the center, upper or lower pole of the rejected kidney; (7) sequential scanning using Yb^{169}-EDTA and/or IOH was of no predictive value in rejection of the kidney transplant; (8) renal clearance studies gave additional information concerning the functional state of the rejected transplant, filtration was elevated in rejection crises; and (9) The Xe^{133} washout determination of the kidney before transplantation was of prognostic value in some cases when the renal cortical blood flow was normal.

A general discussion is given and the authors concur with previous reports in the literature that the use of radioisotopic procedures is justified to determine function and morphology of kidney transplants. —*Charles W. Cooley, M.D.*

Skeletal System

Genuth, Saul M., Klein, Leroy, Rabinovich, S., and King, Katherine C. Osteomalacia accompanying chronic anticonvulsant therapy. *J. Clin. Endocrinol. & Metabol.*, Sept., 1972, *35*, 378–386. (From: Case Western Reserve University, Cleveland, Ohio, and The Toronto Western Hospital, Toronto, Ont., Canada.)

This is a case report of an 18 year old black male, who has been on anticonvulsant medications for 17 years. For at least 10 years the patient's average daily intake of these medications was: phenobarbital 64–96 mg./day, primidone 750–1,000 mg./day, and either diphenylhydantoin or mephenytoin 300–400 mg./day.

The roentgenographic findings were reported as

follows (although no roentgenograms are reproduced in the article): there was widening and demineralization of the femoral, tibial, fibular, and radial epiphyses as well as failure of fusion of the angular epiphyses of the vertebral bodies. Subperiosteal resorption of the phalanges was noted as well as cystic changes in the heads of the humeri and clavicles. A "rugger-jersey" pattern of increased density of the upper and lower borders of the vertebral bodies was also present.

Laboratory findings included serum calcium levels ranging from 7.9–8.17 mg./100 ml., and phosphorus levels ranging from 3.3–4.0 mg./100 ml. The serum alkaline phosphatase was elevated at 60 King-Armstrong units. Other blood chemistries were well within normal limits. There was no aminoacidemia, but there was a mild aminoaciduria. It is to be noted, however, that a urinary aminoacid screening at age 11 was negative.

An open iliac crest biopsy was subsequently performed and revealed the presence of numerous wide osteoid seams covering almost all of the endosteal surfaces of the trabecular bone and the inner aspects of the haversian canals. Quantitation of the osteoid as a proportion of the total bone matrix in the biopsy section demonstrated that 23 per cent of the bone was unmineralized (normal less than 6 per cent). Changes compatible with mild osteitis fibrosa were also present.

The evidence for the osteomalacia was both roentgenographic and histologic, while the evidence for the secondary hyperparathyroidism was not only roentgenographic and histologic, but also chemical as evidenced by elevated serum immunoreactive parathormone suppressible by calcium infusion.

It was concluded that sustained exposure to large amounts of anticonvulsants induced a state of deficient vitamin D, reputedly due to altered metabolism of the vitamin, or inhibition of its effects. Other causes of osteomalacia in this age group which were felt to be excluded by one means or another were dietary deficiency, malabsorption, renal glomerular disease, renal tubular acidosis, a generalized Fanconi syndrome, vitamin D resistant rickets, and finally there was no history of chronic ingestion of fluoride or aluminum hydroxide compounds.

Unfortunately, as in most cases like this, it is not possible to withdraw the anticonvulsive medication without incurring a serious risk of status epilepticus. There are no other recommendations for prophylaxis at this time.—*Donald M. Monson, M.D.*

Fergusson, I. L. C. Haemangiomata of skeletal muscle. *Brit. J. Surg.*, Aug., 1972, *59*, 634–637. (From: Westminster Hospital, London, England.)

Two cases of skeletal muscle hemangiomata are described. Most authors believe that these tumors are congenital in origin and they have frequently been described as vascular hamartomata. Most are discovered in childhood or adolescence and over 85 per cent of the reported cases occurred in the first 3 decades of life. There is an almost equal sex incidence. They mainly arise from a single muscle. Almost all present as a soft tissue swelling. Sixty per cent of cases have associated pain from pressure on local nerves. Overlying skin is frequently normal, but may be warm and bluish red.

Soft tissue roentgenograms may show the appearance of dilated vessels, and also the presence of phleboliths. Arteriography can be valuable in confirming the diagnosis preoperatively and indicating the origin of the feeding vessels.

Microscopically, arterial, venous, capillary and cavernous elements may be found infiltrating between muscle fibers and various degrees of degeneration.

The treatment of choice is local excision of the tumor. Where excision is impracticable because of extensive infiltration or the likelihood of risking permanent deformity, radiotherapy may be beneficial. Partial excision with the risk of recurrence is to be avoided wherever possible.—*David Morse, M.D.*

Blood and Lymph System

Heinze, H. G., Klein, U., Becker, H. M., Bedacht, R., and Rueff, F. L. Angiographie bei abdominalen Strömungsgeräuschen. (Angiography in patients with abdominal murmurs.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, March, 1972, *116*, 306–317. (Address: Priv.-Doz. Dr. H. G. Heinze, Klinik und Poliklinik für Radiologie der Universität, 8 München 12, Ziemssenstrasse 1, Germany.)

Abdominal murmurs can be heard over vascular stenoses, collateral circulations, arteriovenous fistulae and aneurysms. These different causes of abdominal murmurs and their pathophysiologic basis are discussed and illustrated by cases which have been investigated by means of angiography.

Renal artery stenosis is the most common stenosis; a murmur is audible in 30–50 per cent of the cases. Congenital vascular hypoplasia, fibromuscular hyperplasia, arteriosclerosis, endangiitis obliterans, aneurysms of the aorta or renal artery, arterial emboli, compression or kinking of renal arteries and traumatic vascular lesions can all cause a stenosing process of the renal arteries. The poststenotic dilatation is a diagnostic criterion in differentiating a true stenosis from a functional vascular spasm.

Collateral circulation is usually the result of an acquired vascular stenosis; congenital vascular abnormalities with collateral circulation are rarely encountered. Preformed collaterals of the splanchnic arteries are the pancreaticoduodenal arcade between the celiac trunk and the superior mesenteric artery,

and the arc of Riolan between the superior and inferior mesenteric artery. The collateral circulation to the kidney arises from the capsular, peripelvic and ureteral arterial systems. Collateral circulation does not always generate an audible sound; in particular, renal collaterals are found frequently without a murmur.

Aneurysms are primarily due to arteriosclerosis; however, congenital deformities as well as mycotic and traumatic aneurysms have to be considered. They all can cause murmurs. Angiography is usually needed for diagnosis, as splenic artery aneurysms calcify rarely and renal artery aneurysms in only 30–50 per cent of the cases.

Arteriovenous fistulae cause usually a continuous murmur with a systolic maximum. They can result in high output failure when a large amount of blood is shunted. Intraabdominal A-V fistulae are rare; they are iatrogenic, traumatic, spontaneous or congenital in origin. Two cases of A-V fistulae post nephrectomy are presented and discussed; until 1969 only 19 cases had been reported in the literature.

One case of arterioportal fistula is reported; this is a rare vascular abnormality, of which only 57 cases have been found in the literature. One-third of the cases were of iatrogenic origin. Arterioportal fistulae result in portal venous hypertension with gastric and esophageal varices. Therefore, gastrointestinal bleeding and an abdominal machinery murmur in a patient with previous abdominal surgery should warrant angiography which would be diagnostic in this condition.—*Peter F. Winter, M.D.*

Adamsons, Roland J., Kinkhabwala, Mahesh, Moskowitz, Harold, Himmelfarb, Elliot, Minkowitz, Stanley, and Lerner, Bernard. Portacaval shunt with arterialization of the hepatic portion of the portal vein. *Surg., Gynec. & Obst.*, Oct., 1972, *135*, 529–535. (From: Department of Surgery, Downstate Medical Center, Brooklyn, N. Y.)

Progressive deterioration of hepatic function and development of other undesirable metabolic sequelae following traditional portosystemic shunts are felt to be related to the abrupt decrease in total hepatic blood flow and resultant lowering of sinusoidal pressures. Arterial hookup of the hepatic portion of the portal vein following shunting has been experimentally successful in maintaining hepatic blood flow and pressures.

The authors report the results in 7 patients in whom an end-to-side portacaval shunt was combined with arterialization of the hepatic portion of the portal vein by means of an anastomosis between the right gastroepiploic artery and the reopened umbilical vein. This artery was chosen because of its small size, which avoids an abrupt and damaging increase in hepatic portal vein blood flow and sinusoidal pressure. After completion of an end-to-side anastomosis between the gastroepiploic artery and the umbilical vein, the flow in the umbilical vein is not pulsatile, but a thrill is palpable. Postoperatively, a bruit is heard over the arteriovenous anastomosis in the majority of patients, permitting convenient follow-up study of the arteriovenous fistula.

The 7 patients have been followed from 3 to 22 months. One elderly alcoholic patient succumbed of hepatic coma 5 months after shunting. At 3 months postshunting however, when he had been re-admitted with jaundice, the bruit was absent and angiography confirmed occlusion of the arteriovenous anastomosis. Another middle-aged alcoholic died approximately 6 months following shunting of hepatic failure due to fatty metamorphosis caused by continued excessive alcoholic intake and malnutrition. A third young alcoholic died from septicemia following abdominal trauma without hepatic decompensation. He had survived approximately 5 months.

Histologic studies of the livers of the patients who succumbed showed a progression of cirrhosis in 2 patients. Vasculitis, intima proliferation, or thrombosis of the portal vein branches was not observed. These findings demonstrate that arterialization of the liver of 5 to 6 months' duration did not create vascular damage as had been observed in animal experiments.

The other 4 patients have survived from 3 to 22 months with no restriction in protein intake. The most significant feature following arterialization of the liver was the smoothness of the postoperative course in all patients, with no hepatic decompensation, which appears to be the major contributing factor in avoiding operative mortality. There has been no complicating ascites.

This procedure is contraindicated in patients with spontaneous reversal of blood flow in the portal vein. Under these circumstances the portal vein does not contribute to the hepatic perfusion except by providing an outflow tract, and therefore arterialization does not appear justified.

The limited but encouraging experience with arterialization of the hepatic end of the portal vein suggests that it may be used in patients with already existing portacaval shunts in whom hepatic encephalopathy is the major complication.—*Donald M. Monson, M.D.*

Walker, D. I., Bloor, K., Williams, G., and Gillie, I. Inflammatory aneurysms of the abdominal aorta. *Brit. J. Surg.*, Aug., 1972, *59*, 609–614. (Address: Mr. D. I. Walker, Department of Surgery, Manchester Royal Infirmary, Manchester M13 9WL, England.)

Of 187 patients undergoing operative treatment for abdominal aortic aneurysms, 168 were found to have aneurysms of the atherosclerotic type. In the remaining 19 cases the aneurysms were unusually thick-walled and surrounded by extensive fibrous

adhesions which made operative procedures much more difficult. These are described as inflammatory because of the dense infiltration of the medial and adventitial coats with lymphocytes, plasma cells and histiocytes including occasional giant cell forms and small granulomata. They have a thick firm smooth wall which is shiny white in appearance. The adjacent dense fibrosis is marked and may involve adjoining tissues and structures. This makes dissection of adjacent structures such as sigmoid colon, duodenum and inferior vena cava difficult.

Retrospective study reveals certain clinical characteristics of these patients differing from the usual atherosclerotic aneurysm group. The inflammatory aneurysms tended to occur in a younger age group with an age range of 42 to 71 years (average age 62 years) as opposed to the atherosclerotic group with ages ranging from 55 to 86 years (average age 72 years). Whereas 15 per cent of the inflammatory group presented after rupture of their aneurysms, 40 per cent of the atherosclerotic group presented with this clinical finding. The 1:9 female to male ratio for atherosclerotic aneurysms manifested itself in the inflammatory group as well. There was significantly greater peripheral vascular occlusal disease in the atherosclerotic group as determined by pedal pulse absence as compared with the inflammatory group. The erythrocyte sedimentation rate tended to be elevated in the inflammatory aneurysms, whereas it was usually normal in the atherosclerotic group. There was no significant difference in the extent of calcification present as visualized roentgenographically between the groups.

It would appear that inflammatory aneurysms are a discrete entity with significant differences from a more common atherosclerotic form in both their clinicaland structural characteristics.—*David Morse, M.D.*

DI CHIRO, GIOVANNI. Recent successes and failures in radiographic and radioisotopic angiography of the spinal cord. *Brit. J. Radiol.*, 1972, *45*, 553–560. (From: Section on Neuroradiology, National Institute of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, Md.)

Radiographic visualization of the arteries of the thoracolumbar segment of the spinal cord has been consistently obtained since the introduction of the selective arteriographic technique. The successful demonstration of the cervical cord vessels is improved, if, in addition to the vertebral arteries, both costocervical trunks are also injected. Nevertheless, the author fails to adequately visualize the cervical cord vasculature in about 20 per cent of the cases.

Attempts to demonstrate spinal cord vessels in man, by nonselective techniques with potentiation of aortographic methods, have failed.

Visualization of well individualized normal spinal cord veins is rarely obtained.

Some observations made during the author's angiographic studies of 70 cases of arteriovenous malformation of the spinal cord are reported. Technical advice is offered to improve the demonstration of feeders in this frequent pathologic lesion of the spinal cord. The first observation of a cord arteriovenous malformation associated with a similar malformation of the brain is reported. Spinal subarachnoidal bleeding is an unexpectedly rare complication encountered almost exclusively in cases where a concomitant arterial aneurysm is present. In patients suspected of harboring an arteriovenous malformation of the thoracolumbar spinal cord, the dangerous possibility of needle penetration within the lesion should be considered before attempting a lumbar myelography. In some instances, one may pass directly to arteriographic studies avoiding myelography. An alternative screening procedure is the newly introduced radioisotope spinal cord angiography.

Certain angiographic observations in tumors, obstructive vascular disease, trauma, and radiation damage of the spinal cord are commented upon.—*William T. McLaughlin, M.D.*

RADIATION THERAPY

ARSENEAU, J. C., SPONZO, R. W., LEVIN, D. L., SCHNIPPER, L. E., BONNER, H., YOUNG, R. C., CANELLOS, G. P., JOHNSON, R. E., and DEVITA, V. T. Nonlymphomatous malignant tumors complicating Hodgkin's disease: possible association with intensive therapy. *New England J. Med.*, NOV., 1972, *287*, 1119–1122. (Address: J. C. Arseneau, M.D., Bldg. 10, Room 12N226, National Institutes of Health, Bethesda, Md. 20014.)

The case records of 425 patients with Hodgkin's disease treated at the NIH were reviewed. These were divided into subgroups on the basis of treatment received. The expected incidences of malignant tumors were calculated for each subgroup on the basis of age, sex, and mean follow-up period from the time of diagnosis of Hodgkin's disease.

Significantly increased risks of development of second malignant tumors were found in the entire group of 425 patients and in the subgroups, treated with both radiotherapy and chemotherapy, and with intensive radiotherapy without intensive chemotherapy. The greatest increase in risk was observed in 35 patients who received *both intensive radiotherapy and intensive chemotherapy*.

Within the past decade wide-field intensive radiotherapy and combination chemotherapy have become accepted approaches for the treatment of Hodgkin's disease.

The authors have observed, within the past year, 3 cases of a second malignant tumor complicating Hodgkin's disease. These cases were remarkable in that the second tumors occurred in a group of rela-

tively young mean age. Two of the second tumors had unusually malignant histologic characteristics, and all had a rapidly fatal clinical course. The patients in whom these second tumors developed had all received intensive radiotherapy, had recurrent Hodgkin's disease, and had been treated with combination chemotherapy within only a few months after radiotherapy.

Chemotherapy was subclassified as follows: intensive chemotherapy (IC), consisting of MOPP or cytoxan, vincristine, procarbazine and prednisone (COPP) for a minimum of 6 months; some chemotherapy (single drug therapy or multiple agents used sequentially); and no chemotherapy. Radiotherapy was subclassified as follows: intensive radiotherapy (IR), consisting of total nodal irradiation (treatment of all major node-bearing areas and spleen) or extended field irradiation (treatment of primarily involved nodal areas and the contiguous node areas) given as a unified course of therapy; some radiotherapy, comprising local field irradiation restricted to the primary site of disease on one or more separate occasions; and no radiotherapy. The patients treated at the Institute (including all those who received total nodal irradiation and the great majority of those who received extended field irradiation) were given a minimal tumor dose of 3,000 rads to each treatment area.

Of 425 patients with Hodgkin's disease, 19 additional malignant tumors were found in 18. Twelve of these were diagnosed after the diagnosis of Hodgkin's disease and after the initiation of therapy.

The possibility of increased susceptibility to second malignant tumors in patients with Hodgkin's disease has been studied previously, and incidence figures of 2.2 per cent, 1.6 per cent, and 1.8 per cent reported. All previous reports have concentrated on the over-all incidence without analysis of the possible role of therapy in inducing second malignant tumors.

Opinion is divided whether or not patients with Hodgkin's disease have an increased risk that a second malignant tumor will develop over that of the general population.

All 3 second malignant tumors, in the 35 patients treated with IR+IC, developed within or near fields of previous irradiation.—*Stephen N. Tager, M.D.*

Johnson, Sandra K., and Johnson, Ralph E. Tonsillectomy history in Hodgkin's disease. *New England J. Med.*, Nov., 1972, *287*, 1122–1125. (From: Radiation Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md.)

Of 174 patients recently treated for Hodgkin's disease (between 1965 and 1970), a history of tonsillectomy was obtained in 52 per cent. Except for a low rate of tonsillectomy in younger patients, statistically significant variations from the over-all rate were absent when tonsillectomy was correlated with other features such as sex, extent of disease, presence *versus* absence of constitutional symptoms, primary site of involvement and histologic subclassification.

A comparison of patients and matched siblings did not reveal a difference in tonsillectomy rate, although a number of patients with intact tonsils had healthy matched siblings with a history of tonsillectomy. The review failed to demonstrate a relation between tonsillectomy and the clinical features of Hodgkin's disease. It did not support the hypothesis that prior tonsillectomy increases susceptibility to this disease by removal of a "lymphoid barrier." Also of interest were 2 sibling pairs without tonsillectomy in whom Hodgkin's disease developed coincidentally within a span of 1 year despite separate residences.

Half of the patients had at least 1 sibling with a different tonsillectomy history, and 32 per cent of the closest matched siblings had a tonsillectomy history different from that of the patient with whom they were matched. Of particular interest were 7 patients with intact tonsils whose matched healthy siblings had undergone tonsillectomy.

This review provides the first description of tonsillectomy history correlated with multiple clinical features of Hodgkin's disease.

Under any circumstances, the low rate of familial coincidence observed scarcely warrants the isolation of patients from other members of the immediate family any more than from society in general.

The clinical features of Hodgkin's disease do not support the contention that tonsillectomy selectively predisposes to the clinical expression of this lymphoma.—*Stephen N. Tager, M.D.*

RADIOISOTOPES

Nelson, Jerald C. Effect of increased iodine intake on the thyroidal response to TSH stimulation. *J. Nuclear Med.*, Nov., 1972, *13*, 828–833. (Address: Department of Medicine, Loma Linda University School of Medicine, Loma Linda, Calif. 92354.)

Thyroid response to thyrotropin (TSH) is a test of thyroid function. The thyroidal radioactive iodine (RAI) uptake is the most useful test of this response. Iodine depletion increases the RAI uptake and increases the thyroidal response to thyrotropin (TSH), while iodine excess decreases the RAI uptake and may decrease the response to TSH.

The author studied the effect of increased iodine uptake on the response of the RAI uptake to TSH stimulation. The study compared the response to TSH stimulation of subjects living in southern California, who have a relatively high iodine intake, with a previously reported study of subjects living in Alabama, with lower iodine intakes.

The study included 57 euthyroid subjects, 66 patients with primary hypothyroidism and 19 patients with hypothyroidism due to pituitary failure;

24 hour uptake measurements were made. Each subject received either 5 USP units of bovine TSH intramuscularly once, or 10 units daily for 3 days. Eighteen hours after the final injection of TSH, background counts were obtained and a larger tracer dose of I^{131} for the post-TSH 24 hour thyroidal uptake was given. The calculated mean iodine intake was 359 μg. per day for the euthyroid Alabama subjects and 1,260 μg. per day for the California subjects.

The pre-TSH uptakes and the post-TSH uptakes and increments in uptake were significantly lower in subjects with higher iodine intake when a single dose of TSH was used. The post-TSH uptake and increments after 3 doses of TSH were not significantly different between the 2 groups despite an apparently larger increment in the higher iodine intake group.

There were no significant differences in the hypothyroid patients in the pre-TSH RAI uptake and the post-TSH RAI uptake, or the increments in uptake between the California and Alabama patients. There was no difference in response between the 1 and 3 dose tests. The results in the patients with pituitary failure were the same in California and Alabama.

Increased iodine intake decreases both the pre- and post-TSH RAI uptake when one dose of TSH is given. The increment in RAI uptake after 1 dose of TSH is independent of the level of RAI uptake before stimulation but is decreased when iodine intake is increased. The effect of increased iodine intake disappears after 3 doses of TSH. An absolute increment in 24 hour RAI uptake of 10 or more after TSH stimulation provides a useful dividing line for distinguishing euthyroid responses from the response in primary hypothyroidism in subjects with differing levels of iodine intake after either 1 or 3 doses of TSH.—*Charles W. Cooley, M.D.*

Liuzzi, A., Keaney, J., and Freedman, G. Use of activated charcoal for the collection and containment of ^{133}Xe exhaled during pulmonary studies. *J. Nuclear Med.*, Sept., 1972, *13*, 673–676. (From: Lowell Technological Institute, Lowell, Mass., and Yale University School of Medicine, New Haven, Conn.)

Xenon 133 gas, widely used for pulmonary studies, can be an internal as well as an external source of radiation exposure for medical and paramedical personnel working in the area of its use. A simple method is presented for the collection and containment of Xe^{133}, which takes advantage of the high absorbability of activated charcoal for xenon. Efficiency of xenon collection and containment was studied as a function of temperature.

The basic trap unit consists of a cylindrical glass vessel containing 100 grams of loosely packed activated carbon granules with a glass tube running axially the length of the vessel and excluding the charcoal. A moisture pretrap consisting of a glass cylinder filled with calcium sulfate (drierite) is connected integrally to the inlet to avoid moisture condensation on the charcoal.

In the testing procedure, vacuum pumping was used to draw gases through the tube system at a rate of approximately 6 liters/minute, which simulates the respiratory minute volume of normal humans.

Collection efficiency was studied under 3 cooling conditions, room temperature, ice and water, and dry ice and methanol. In all cases, the efficiency exceeded 99 per cent. Retention is seen to increase at decreased coolant temperatures.

Following the Xe^{133} collection, each trap was then imaged with a Pho/Gamma III scintillation camera to obtain integral counting rates as well as scintiphotographs showing the spatial distribution of the activity within each trap. This demonstrates that with continued bulk flow through the trap, xenon will migrate in the direction of the bulk gas flow. The effect of the activated carbon is to selectively slow down the net flow rate of the xenon.

The trap system has been used in a number of perfusion studies with humans, so that efficiencies could be determined and compared with the experimental results. The system was similarly used in a number of pulmonary experiments with dogs, employing a full face mask. In all cases the computed efficiencies were comparable to those obtained experimentally.

The results clearly indicate the feasibility of using activated charcoal as a means of controlling the escape of radioactive xenon employed in clinical pulmonary studies. Since the trap works quite well at room temperature, a collection system may not require the complexity associated with a cooling requirement.

A technique for recovering the xenon from the trap for re-use is described.—*William T. McLaughlin, M.D.*

Miale, August, Jr., Rodriguez-Antunez, Antonio, and Gill, Wilfred M., Jr. Pancreas scanning after ten years. *Seminars in Nuclear Med.*, July, 1972, *2*, 201–219. (From: Nuclear Medicine Service, Jackson Memorial Hospital, and Division of Radiotherapy and Nuclear Medicine, Cleveland Clinic Foundation, Cleveland, Ohio.)

The pancreas is a difficult organ to study in a clinical setting. Advanced disease usually is present before diagnosis is confirmed by conventional methods.

Although Se^{75} methionine was introduced 10 years ago, progress in using this tracer for study of pancreatic disorders has been slow.

The various chemical, radiologic, ultrasonic, and endoscopic diagnostic approaches all have one or another drawbacks. None has the potential for pro-

ducing images of pancreatic tissue in both an anatomic and physiologic context with the simplicity, speed, safety, and availability of the pancreas scan. Of greater significance is the potential of the scan for use as a screening procedure to initiate an attack on the poor statistical results in pancreatic carcinoma.

The early use of pancreas scans in patients with less than classical signs and symptoms of a pancreatic lesion is stressed as having significant potential. The pancreas scanning as a useful procedure has been much maligned, but detailed analysis of the literature and the authors' own experience show substantial justification for the clinical usefulness and reliability of this method.

The use of the rectilinear scanner in the early half of the decade, in spite of its limitations, led to later and now more widespread use of the scintillation camera for pancreas scanning. The ability of the camera to produce frequent sequential images of the pancreas probably has been the most significant factor in stimulating a revival of interest and clinical use of pancreas scanning.

Digital data processing and short half-life Se^{73} labeled methionine, when available, may lead to another boost in utilization and accuracy.

Successful results require careful technique and a systematic approach. The use of a stimulating meal following an overnight fast is recommended. Interpretation is based on application of relatively well-defined criteria and requires some degree of experience. Much of what was called equivocal or poor results in the past can be explained by an understanding of pancreatic physiology and the actual functional condition of the patient's pancreas.

Clinical results show that a normal study is very strong evidence for lack of pancreatic disease, while abnormal studies are only slightly less accurate in the presence of carcinoma or pancreatitis. The incidence of false negatives and false positives is higher when the rectilinear scanner is used rather than a scintillation camera.—*William T. McLaughlin, M.D.*

ULTRASOUND

Thijs, L. G., Roos, Peter, and Wiener, Jan D. Use of ultrasound and digital scintiphoto analysis in the evaluation of solitary thyroid nodules. *J. Nuclear Med.*, July, 1972, *13*, 504–509. (Address: L. G. Thijs, Department of Internal Medicine, Academisch Ziekenhuis der V.U., 1117 de Boelelaan, Amsterdam 1011, The Netherlands.)

One hundred and two patients with clinically solitary thyroid nodules were examined with a gamma camera and with B-scan ultrasound techniques. Scintiphotos were made 1 hour after an oral dose of $Tc^{99m}O_4$, the position of the nodule being marked on the skin during palpation preceding scintiphotography. The ultrasonograms were obtained with a 2.5 MHz probe and, in general, a single scan obtained over about 15 minutes was performed. Sensitivity was set at a "low" value, because the authors were only interested in the outline of the gland or nodule.

Fifty-three patients, all of them euthyroid, showed a cold area on a scintiphoto corresponding to the nodule. In almost all these cases the outline of the nodule could be made out on the ultrasonic tomogram. Thirty-three patients had a single hyperthyroid nodule. Normal thyroid tissue was completely suppressed in 16 of the 33 patients, so the true size of the gland in these patients could only be assessed by ultrasound. In 13 patients, a solitary nodule was palpable, but delineated on the scintiphoto either by size (8 patients) or not at all and would, therefore, be considered a warm nodule. The ultrasonogram showed that these nodules were thicker than the surrounding tissue and therefore hypofunctioning per unit volume, and should consequently be considered as cold nodules. In 3 patients, a slight indentation formed the only scintigraphic clue to the presence of a nodule. The ultrasonogram showed the presence of a nodule situated almost entirely outside the gland. Using palpation, scintigraphic techniques, and ultrasound data, these nodules were correctly classified as nonfunctioning.

The authors consider that ultrasound is of value in the diagnosis of thyroid tumors: since it can distinguish between solid and cystic lesions; enables one to diagnose some cold lesions which have a deceptive scintigraphic appearance; and gives a more accurate idea of the anatomic shape of the lesion, because depth as well as width and length are displayed.—*Roger C. Sanders, M.R.C.P., F.F.R.*

Pridie, Ronald V., Behnam, Ramsay, and Wild, John. Ultrasound in cardiac diagnosis. *Clin. Radiol.*, April, 1972, *23*, 160–173. (From: Department of Clinical Cardiology, Royal Postgraduate Medical School, Hammersmith Hospital, London W.12, England.)

This article is a review of the cardiac applications of diagnostic ultrasound. It deals particularly with pericardial effusion, the mitral valve, atrial myxomas, aortic regurgitation, and hypertrophic obstructive cardiomyopathy.

The diagnosis of pericardial effusion is made by distinguishing between echoes derived from the anterior chest wall and the pericardium. Separate echoes from the pericardium will not be seen if no pericardial fluid is present. The diagnosis of pericardial effusion from posterior wall pericardial echoes is considered by the authors less reliable, since false positives do occur.

The normal movements of the mitral valve are described; in each cardiac cycle, there are 2 opening (upward) movements and 2 closing movements, 1 partial and 1 complete. The first opening movement

occurs after the T-wave of the electrocardiogram at the onset of ventricular diastole. The second opening movement follows atrial contraction occurring after the P-wave of the electrocardiogram; the second closing movement follows the QRS complex which starts ventricular systole. In mitral stenosis, the diastolic closure rate is reduced. Patients with tight mitral stenosis all have closure rates less than 2.5 mm. per second and the very severe less than 10 mm. per second. The diastolic closure rate is also slowed by hypertrophic obstructive cardiomyopathy and in the presence of aortic regurgitation. The authors have found the technique of value in differentiating mitral stenosis from the Austin Flint murmur and in determining the degree of mitral stenosis when the predominant clinical signs are those of mitral regurgitation. If the anterior mitral cusp is calcified, a thickened echo pattern is seen. Mobility can also be assessed by ultrasound, and the usual range is between 1.7 and 2.5 cm. If a valvotomy is performed with thick immobile valves, the prognosis is poor and the restenosis rate is high. The extent of valve calcification and pliability is better assessed by ultrasound than by radiologic techniques.

The ultrasonic pattern in atrial myxomas is quite characteristic. Below the anterior mitral cusp echo, numerous spotty echoes occur. The diastolic closure is variable, being normal or somewhat slowed.

In the authors' experience, examination of the aortic valve motion is of little value; in aortic regurgitation there may be some vibration of the anterior mitral cusp due to the jet of blood regurgitating through the incompetent aortic valve. There may also be premature closure of the mitral valve where aortic cusp perforation has followed bacterial endocarditis.

In mitral regurgitation, the diastolic closure rate is accelerated; in combined stenosis and regurgitation, a biphasic pattern is seen. A rapid diastolic closure rate is not diagnostic of mitral regurgitation, but can be seen in any condition where there is a raised left atrial pressure, as with constrictive pericarditis or traumatic pericardial effusion.

In hypertrophic obstructive cardiomyopathy (IHSS), some mitral regurgitation is usual. In addition, there is an increased septal echo and an anterior systolic movement of the anterior mitral cusp. These characteristics make it possible to make a diagnosis of IHSS without catheterization.

The authors briefly mention the measurement of left ventricular volumes by measuring the mitral ring movement and the difference in left ventricular diameter as measured by ultrasound from the fourth or fifth left intercostal space. Such a measurement has been found to correlate well with angiographic data.

This review must be considered limited, because many of the applications of ultrasound to cardiac diagnosis have been described since the article was written; in particular, there is no mention of its use in congenital heart disease.—*Roger C. Sanders, M.R.C.P., F.F.R.*

Rasmussen, S. Nørby, Holm, H. H., Kristensen, J. Kvist, and Barlebo, H. Ultrasonically-guided liver biopsy. *Brit. M. J.*, May, 1972, *2*, 500–502. (From: Ultrasonic Laboratory, Department of Surgery and Department of Pathology, Gentofte Hospital, DK-2900 Hellerup, Denmark.)

A 2 MHz transducer with a central canal with an internal diameter of 2.5 mm. was used for a series of 18 liver biopsies. After the skin had been sterilized and local anesthesia and sterile oil had been applied, a guide needle was passed *via* the central canal of the transducer to a depth corresponding to the thickness of the abdominal wall. An aspiration needle was then inserted through the guide needle and passed in the direction of a previously located lesion to a marked-off depth. The duration of the intrahepatic stage of the procedure was about 5 seconds.

Both the ultrasonic aspiration technique and blind biopsy using the Menghini technique were performed in 18 patients. Thirteen of the 18 patients were found to have liver metastases either by biopsy, operation, or necropsy. Three patients were found at autopsy not to have liver metastases and in 2 a definitive diagnosis could not be made. Only 3 of the 13 patients with tumors had positive biopsies using the Menghini technique. Nine of the biopsies taken with ultrasonic aspiration technique were positive, and in 2 others the findings were "possible tumor cells." The only complication was 1 case of simple pneumothorax which did not require treatment. Since a needle of only 2.6 mm. in diameter was used for aspiration, only detached cells could be examined cytologically. This information is not as comprehensive as that gained with the Menghini needle but is, in the authors' opinion, usually adequate to diagnose malignancy.

The authors conclude that, if a lesion can be located within the liver ultrasonically, aspiration biopsy under the guidance of ultrasound much increases the accuracy of liver biopsy.—*Roger C. Sanders, M.R.C.P., F.F.R.*

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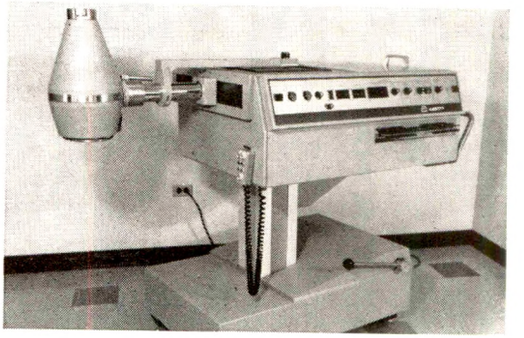


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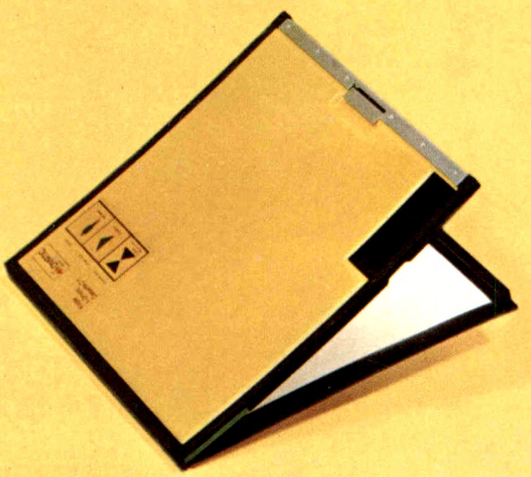
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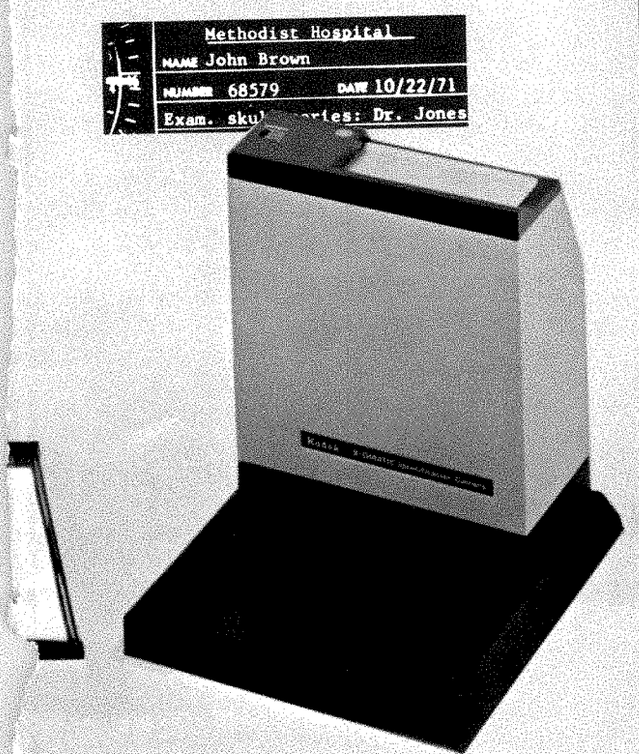


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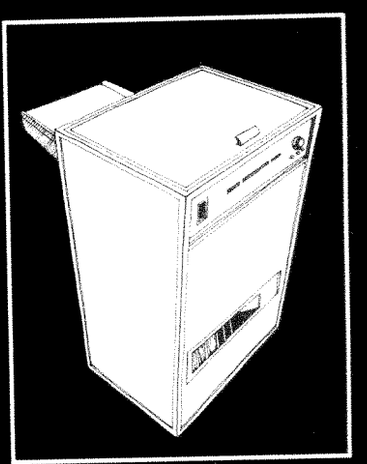
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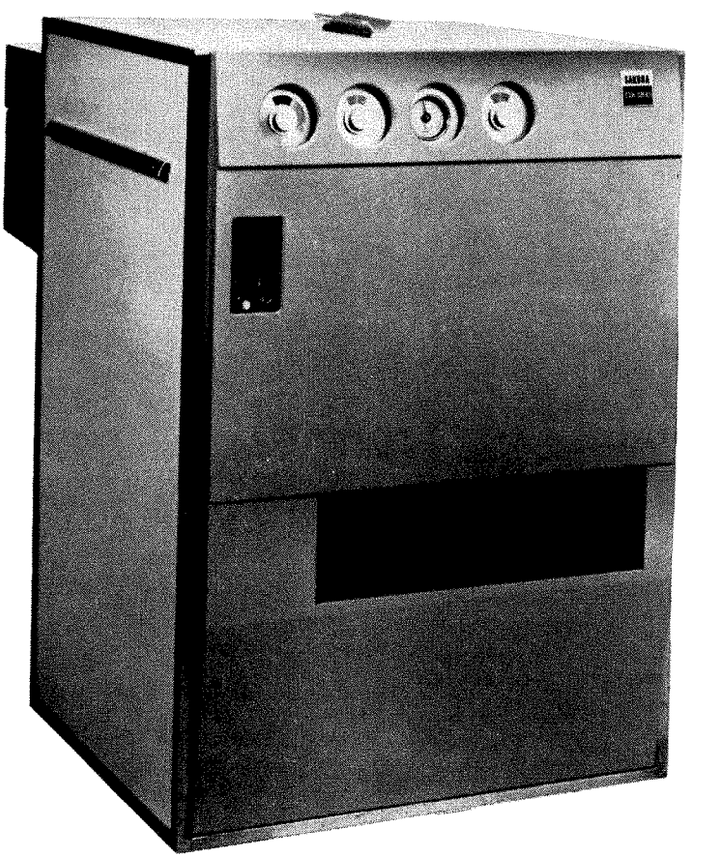
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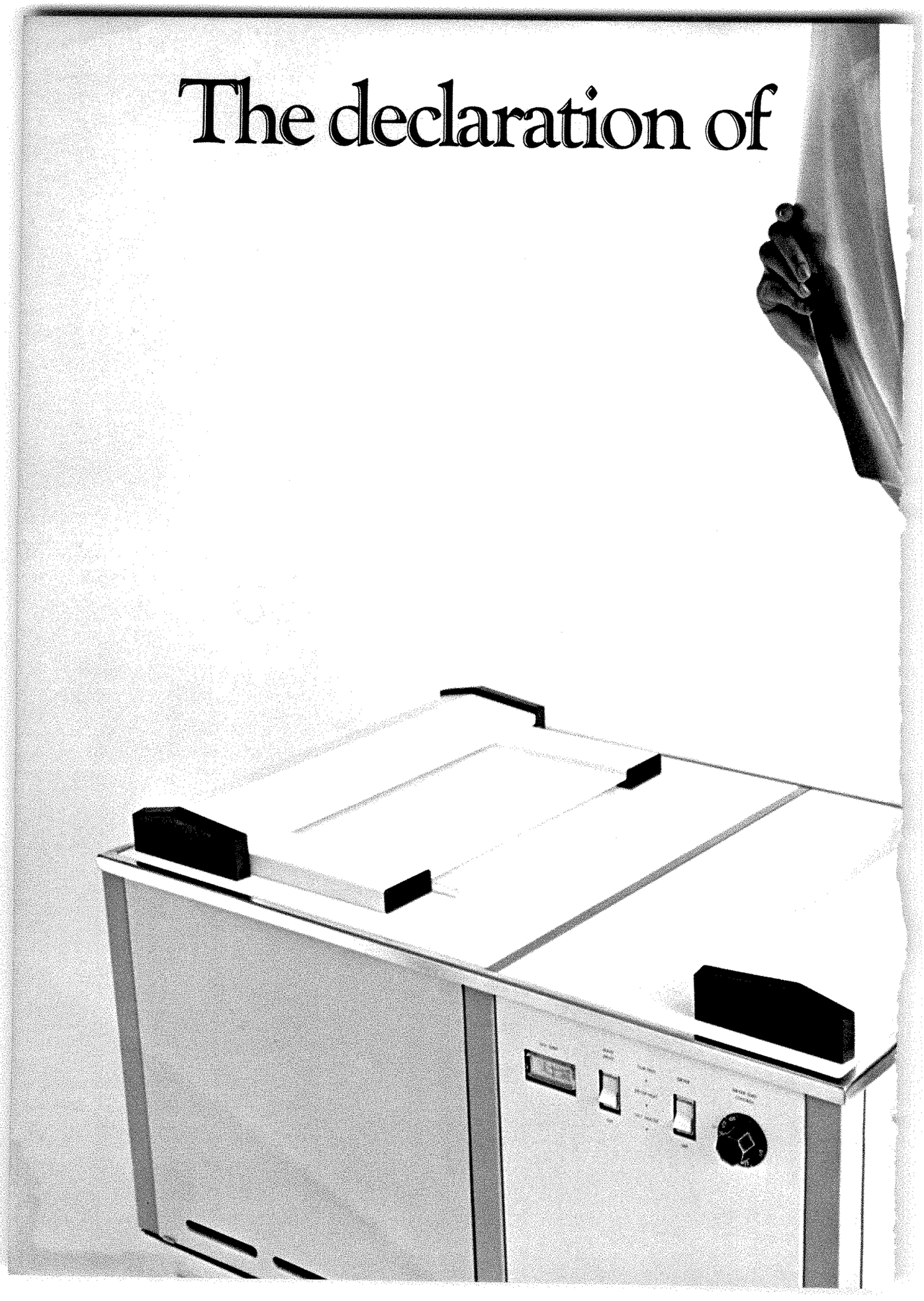
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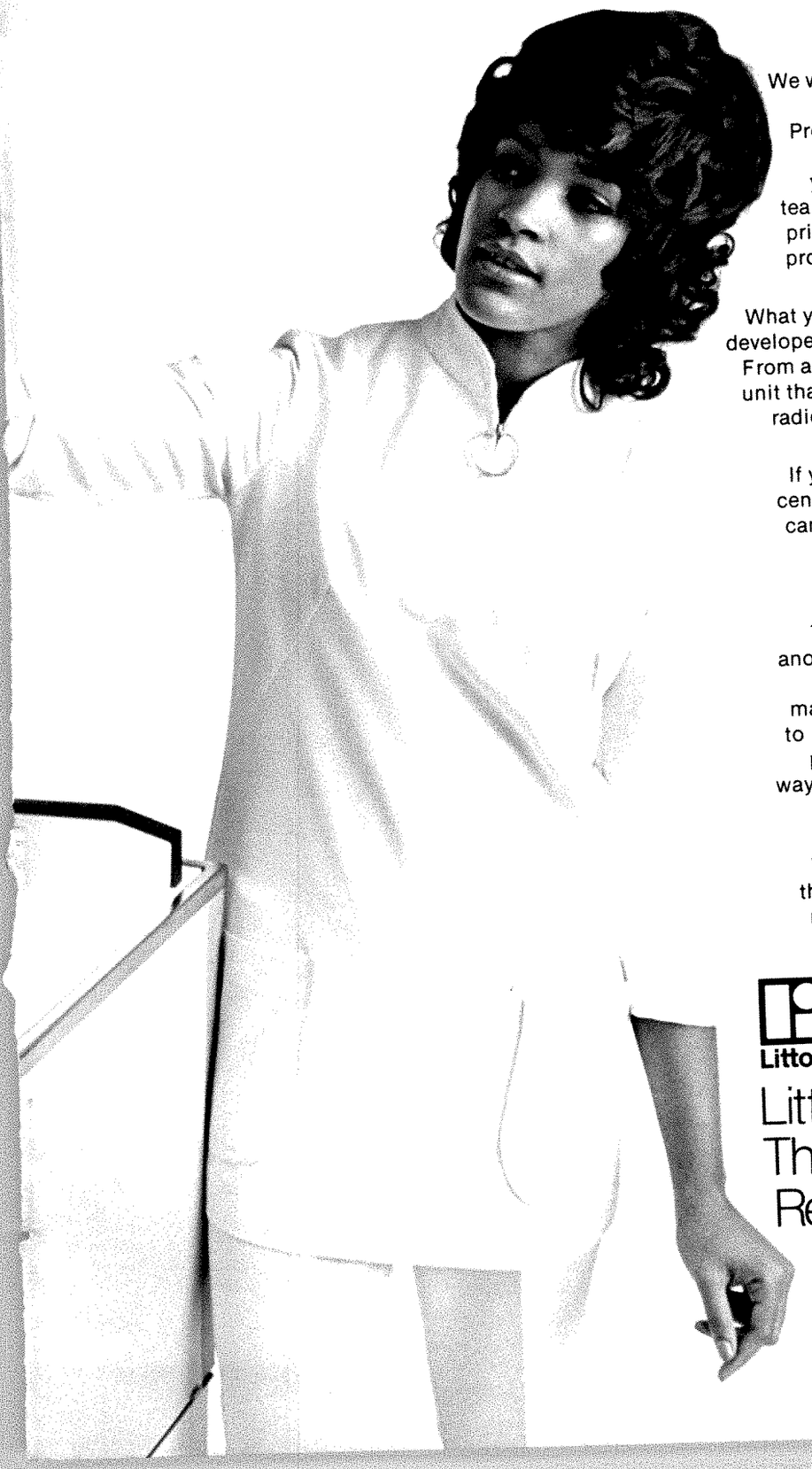
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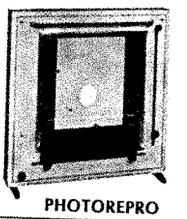
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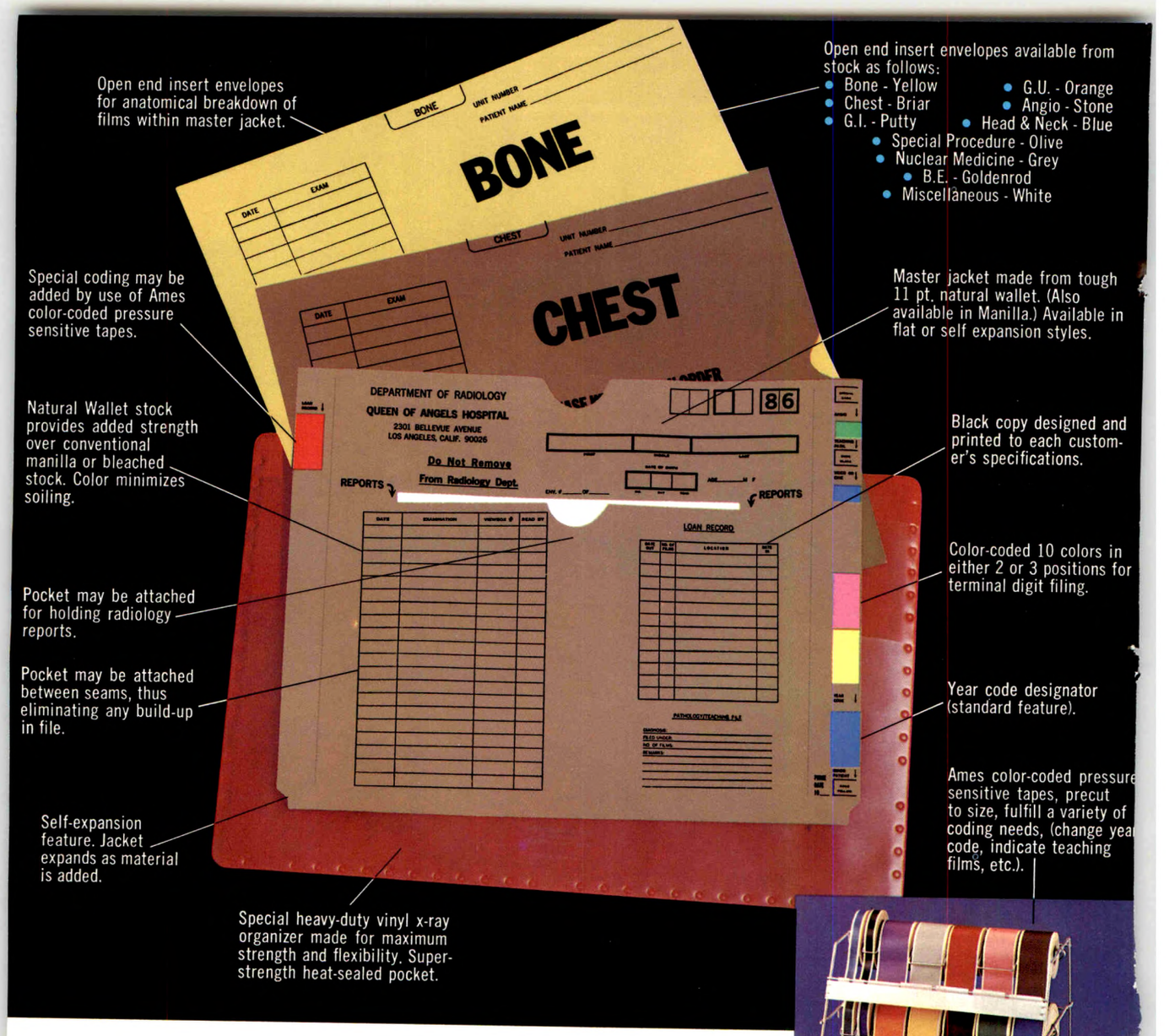
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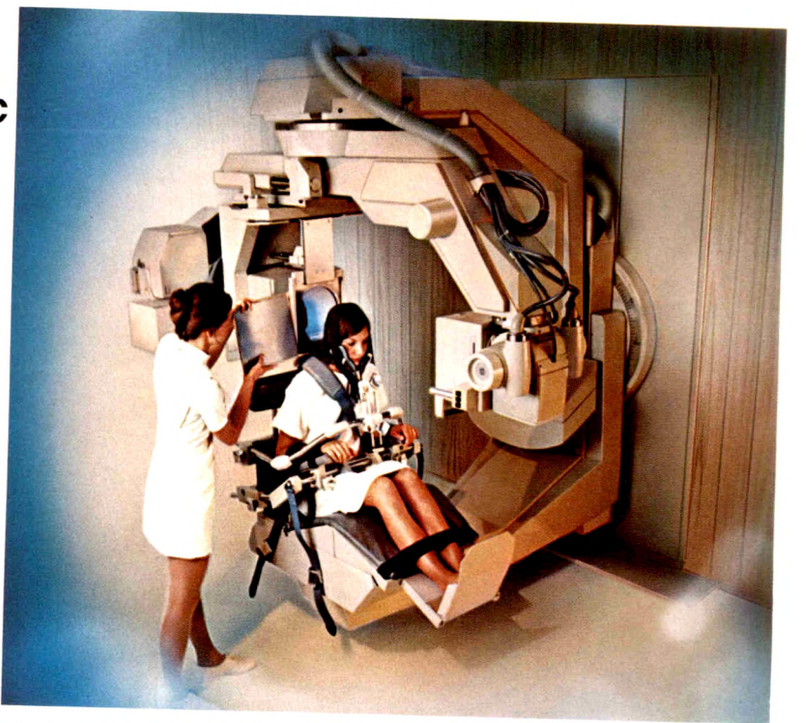
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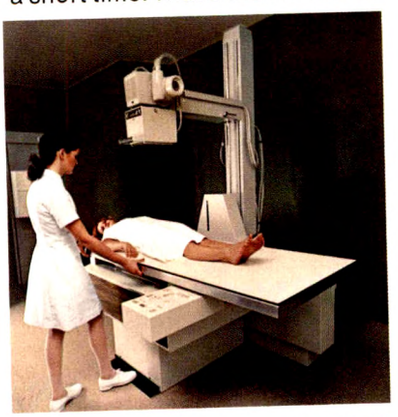


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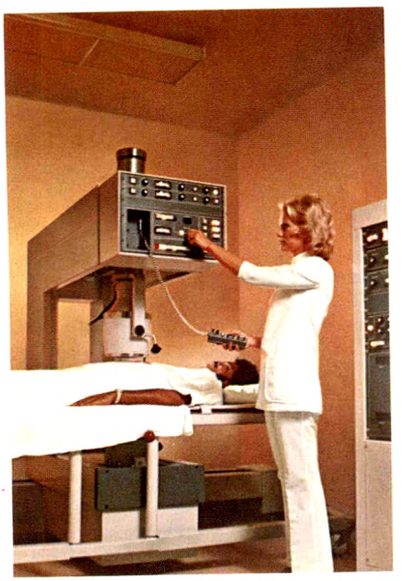


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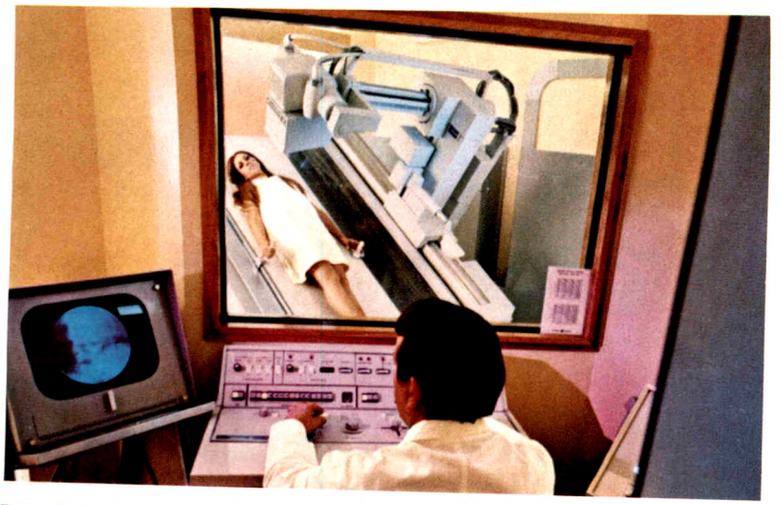
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Maxiscan's two probes scan an entire organ, such as the lung, top and bottom, without turning the patient. The top probe angulates through 270° and travels 12 inches vertically. With optional vertical plane scanning, upright patient scans can be accomplished, plus vertex views of the brain with the patient reclining normally.

Count quantification, by shades of gray or fully functional color over the complete scan area, is attained with the system's Videodisplay and Processing Unit. Recorded patient counts, stored in the memory, are displayed on the video screen; can be manipulated to enhance image details for diagnosis.



Multi-function system assures anatomical coverage

Diagnostic views of all areas of the body—even those which were formerly difficult to see—are easily attained using GE's Telegem™ 90 system.

This total-remote system integrates radiography and fluoroscopy, plus true linear tomography and zonography. It also features a technic called anatomical variance fluoroscopy which, in effect, rotates a patient by video instead of by hand. To accomplish this, the tube unit angulates to 40° longitudinally and to 15° laterally, while the under-table intensifier moves longitudinally to maintain beam centering.

For scanning, the intensifier and tube unit move together through 20 inches. At this travel limit, the top automatically moves up to 80 inches for extended scanning technics.

Telegem 90 also features instant procedural changeover and intermixing of procedures. Plus a top, on the 90°-90° table, which moves six ways, including vertical travel for magnification technics.



Reporting system saves hours

Before Raport™, GE's radiological reporting system, one 450-bed hospital required up to 48 hours to complete each radiological report.

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Image system sets new standards of quality

General Electric's Fluoricon® 300 image system, with its cesium iodide image tube, is setting new standards of image quality in hospitals across the country.

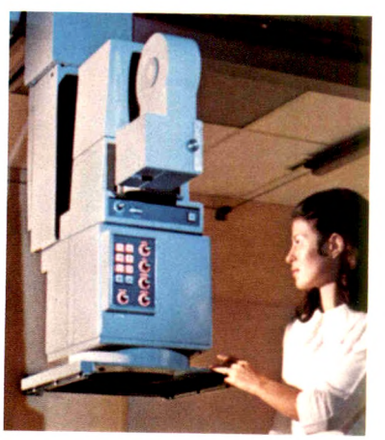
Equally impressive is the performance of the system's wide choice of recording media.

Video tape is integral at enhanced levels; produces diagnostic quality. Also, use VTR at normal levels for back-up recording.

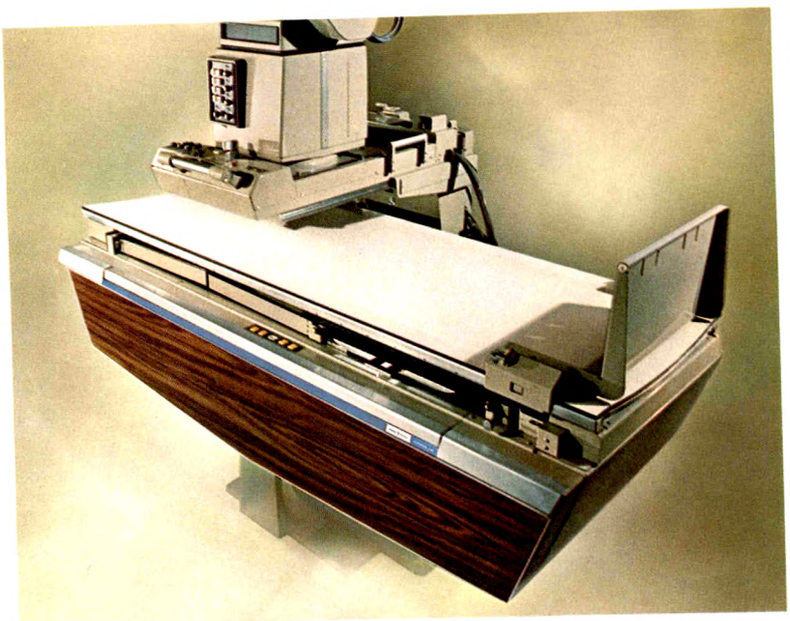
Cine capability offers a choice of 35 mm cameras—with standard or rapid frame rates. Also, GE's Cine 180 provides more than double the per-frame recording area compared with standard 16 mm cine, plus frame rates up to 240 per second.

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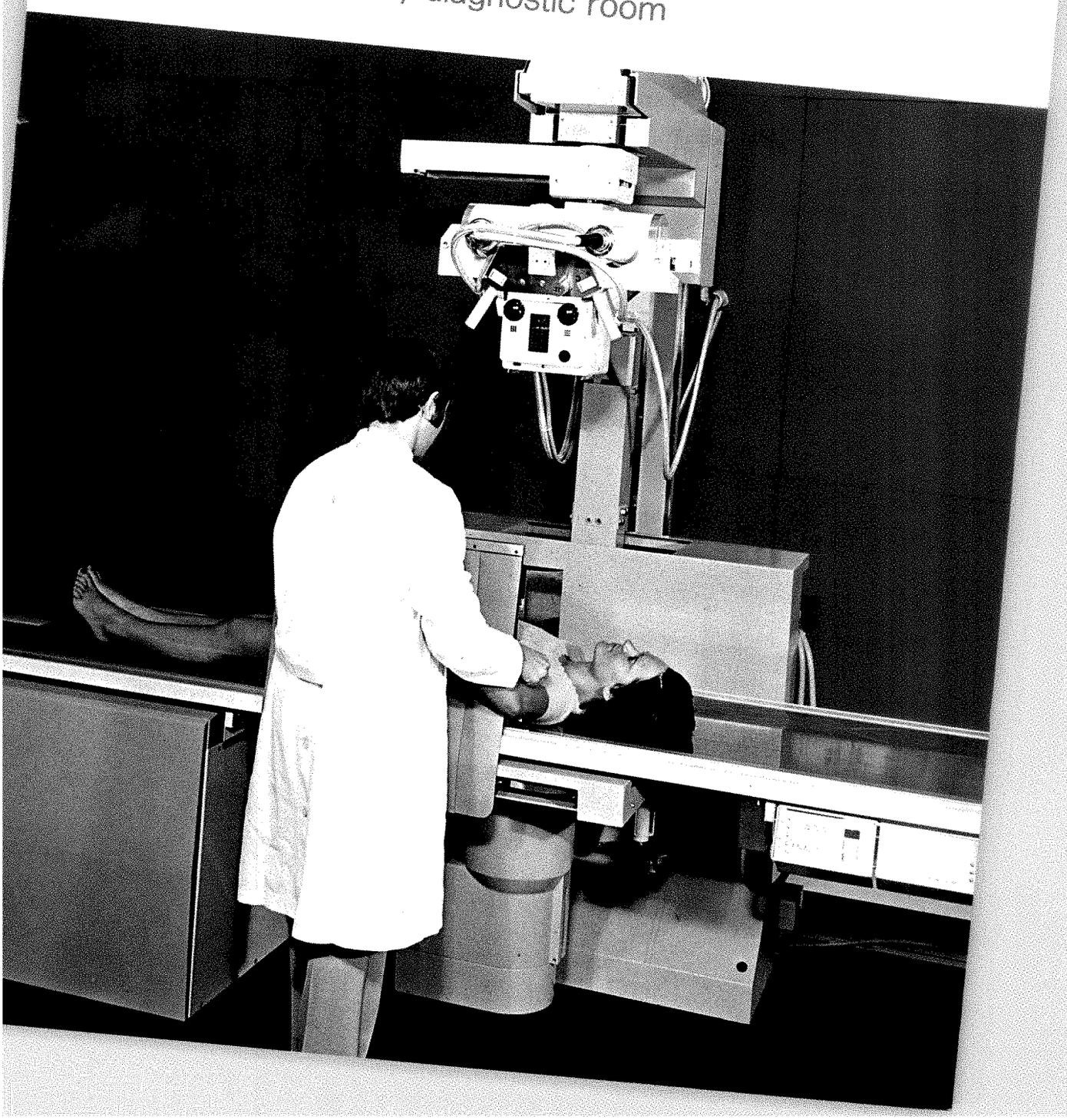
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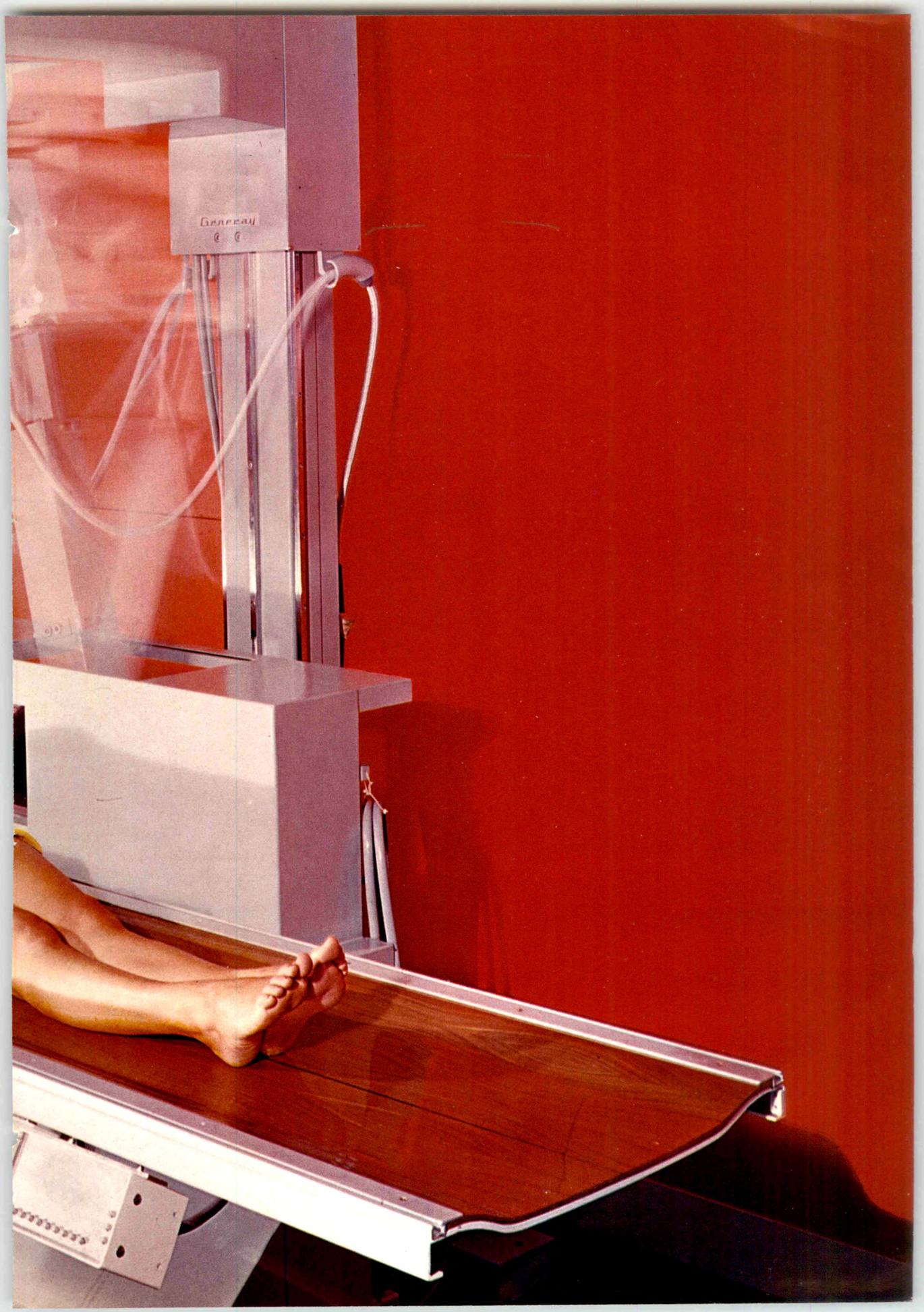
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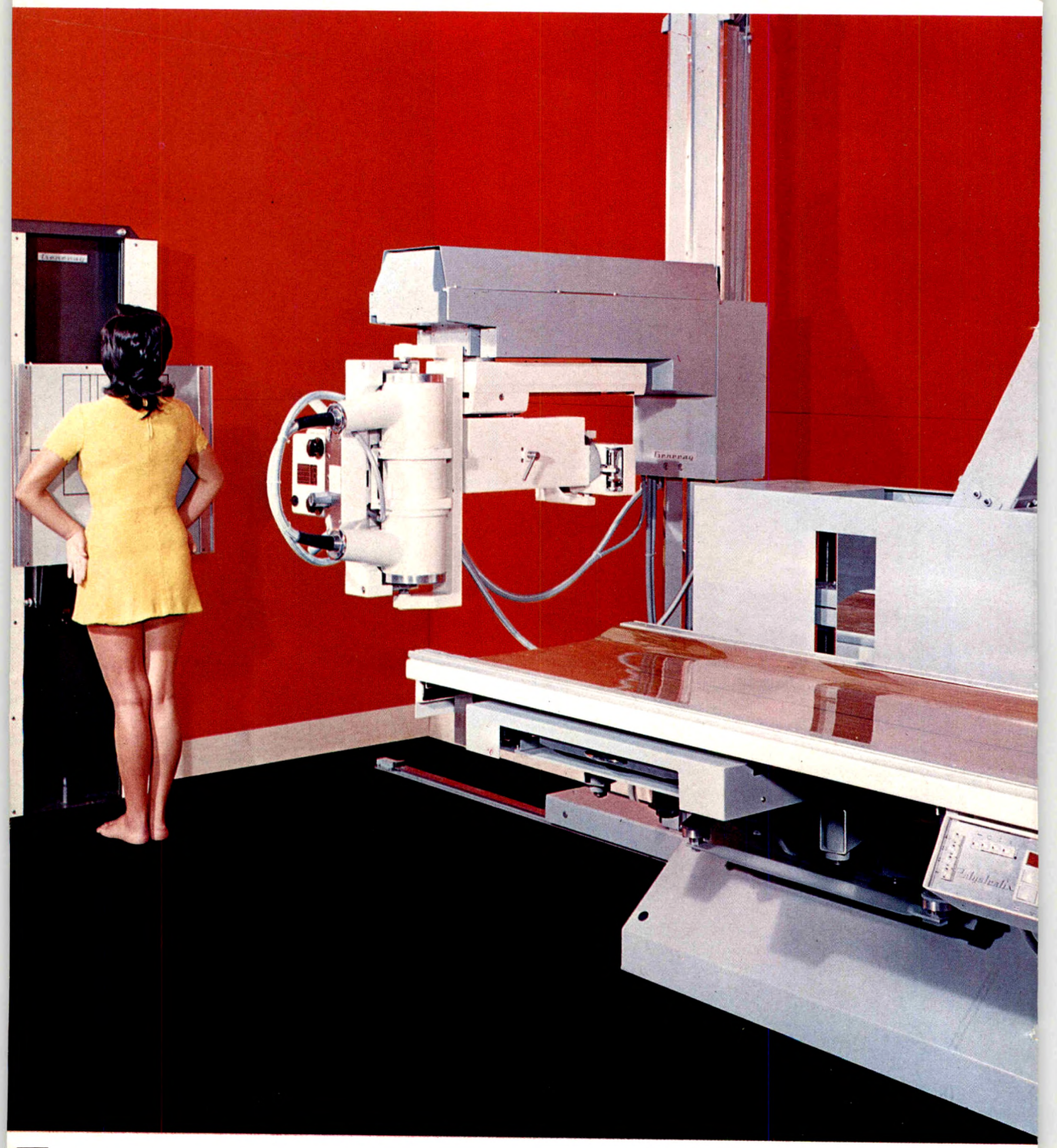
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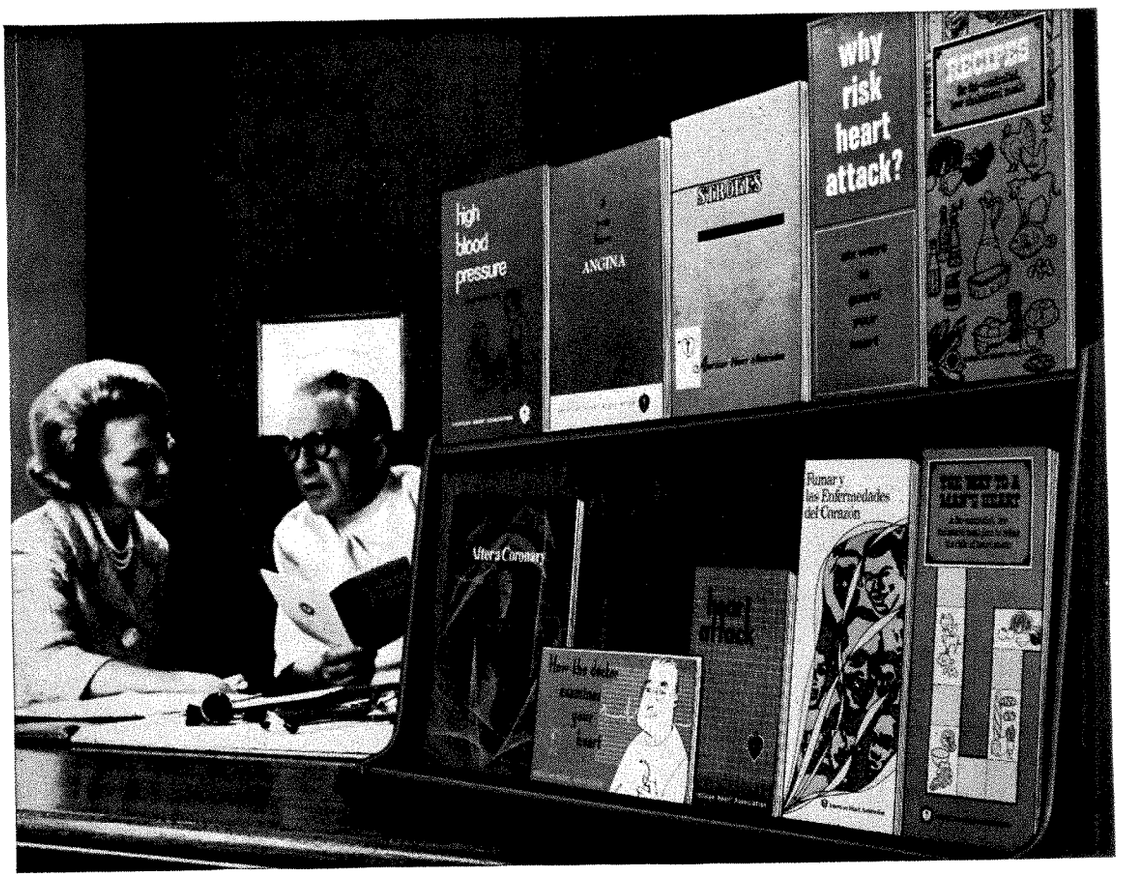
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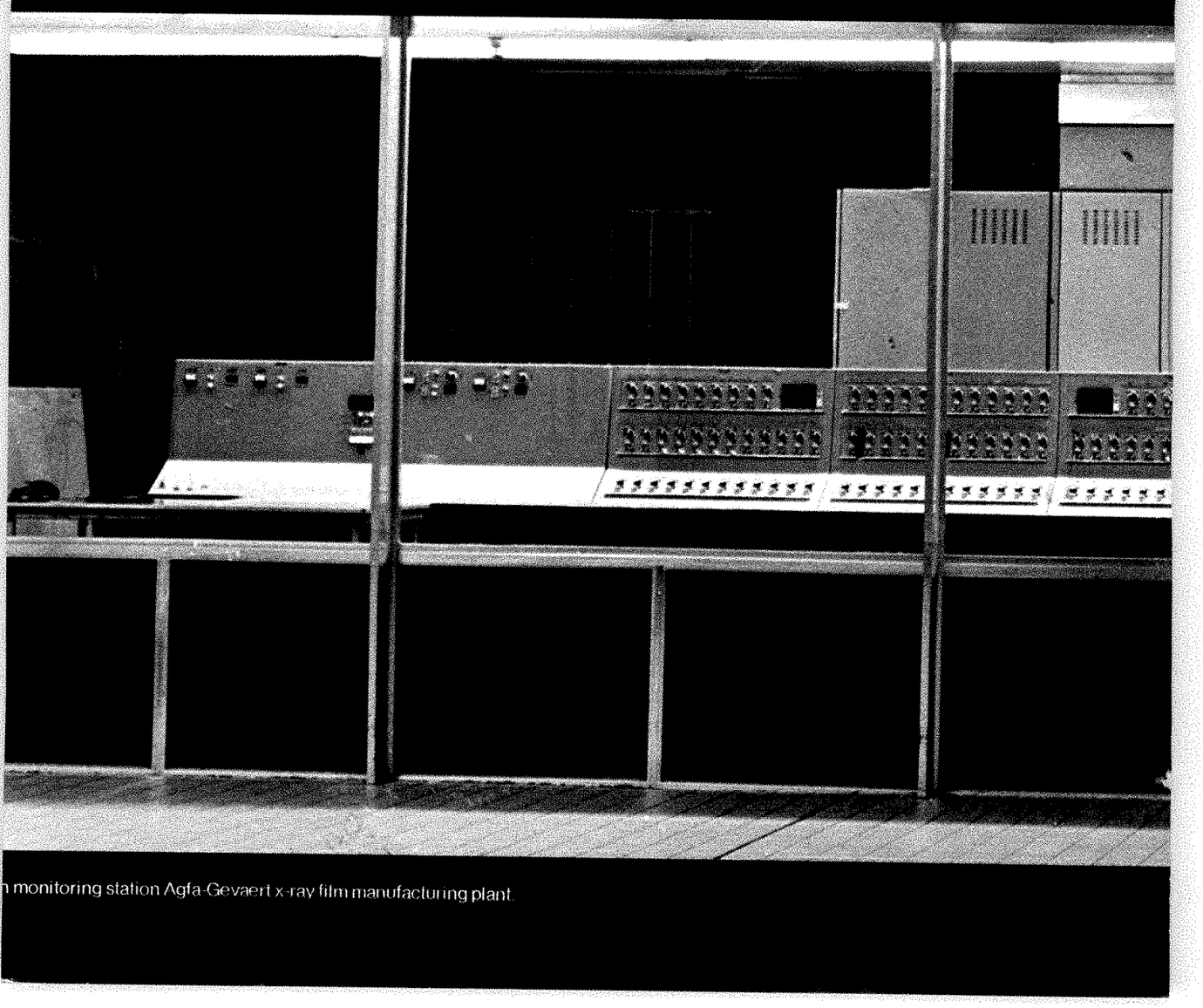
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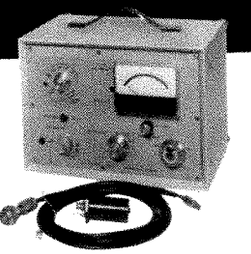
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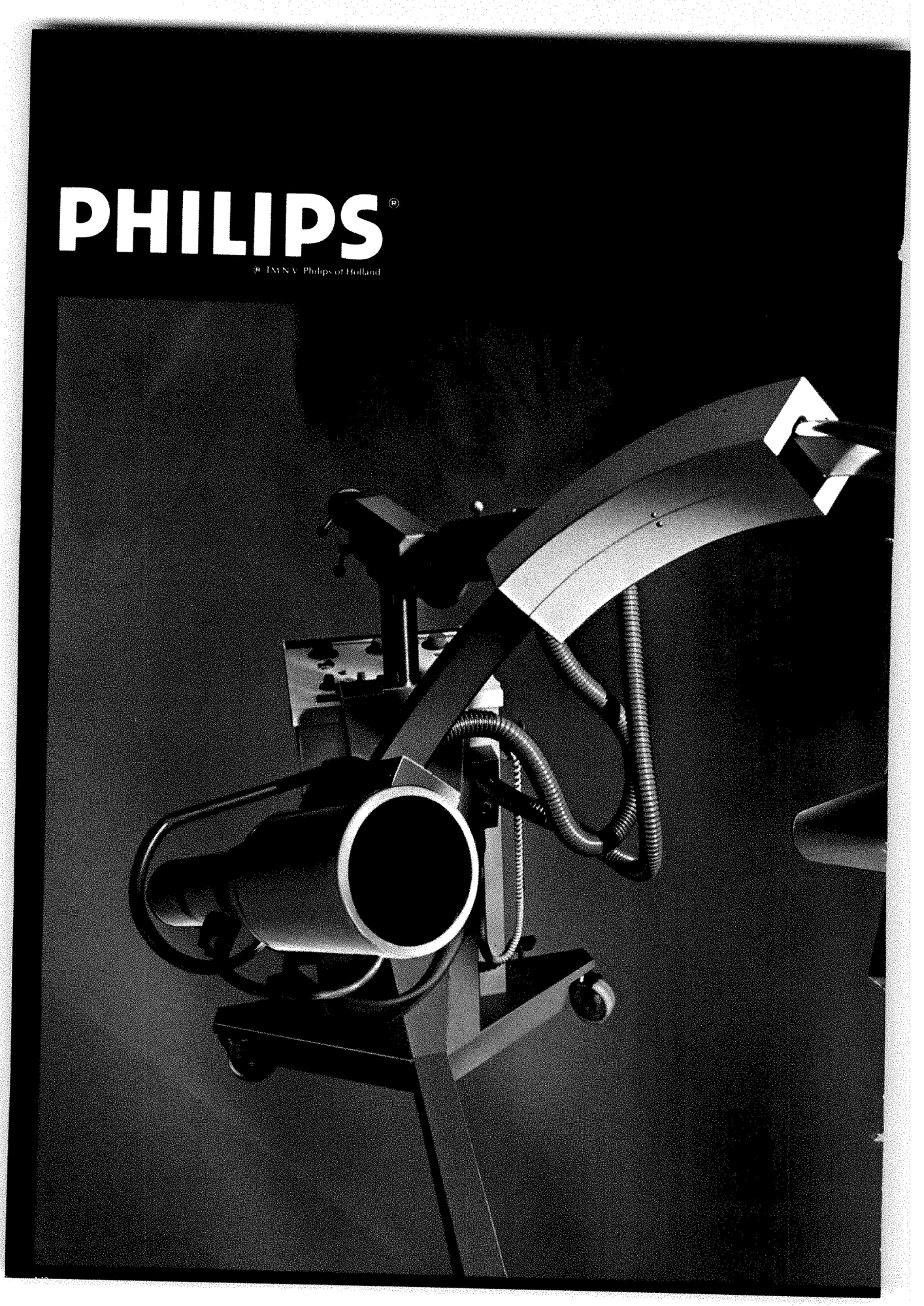
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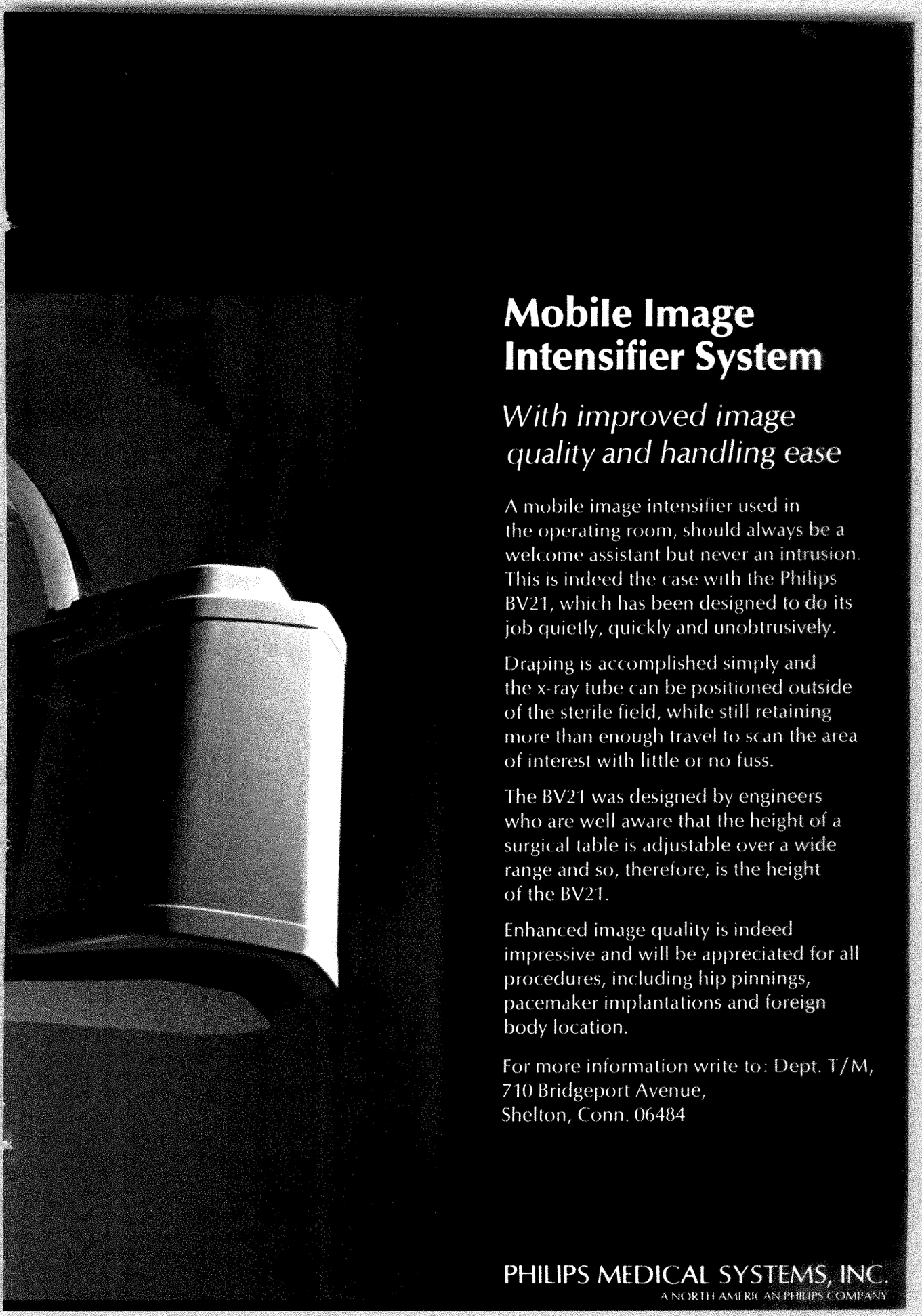
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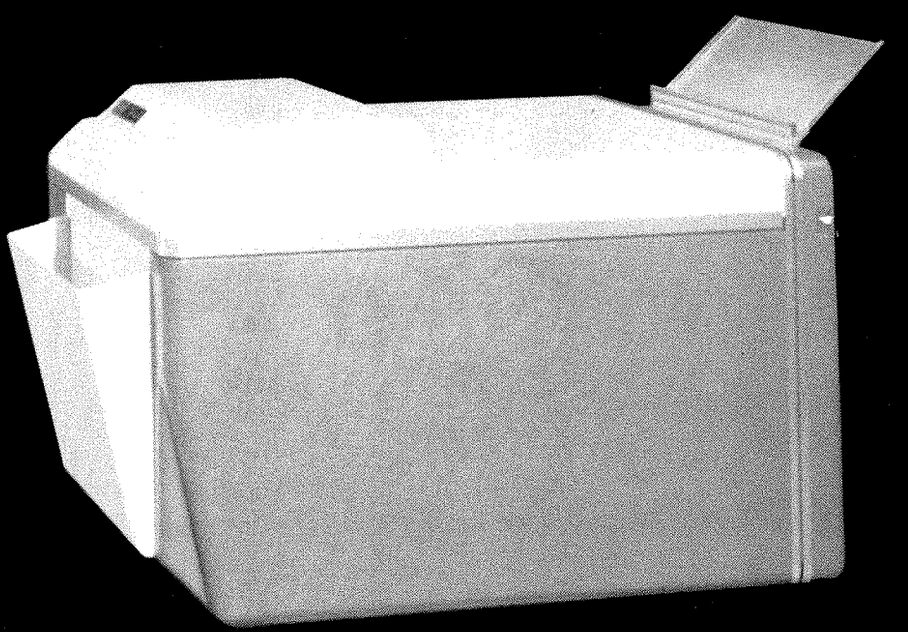
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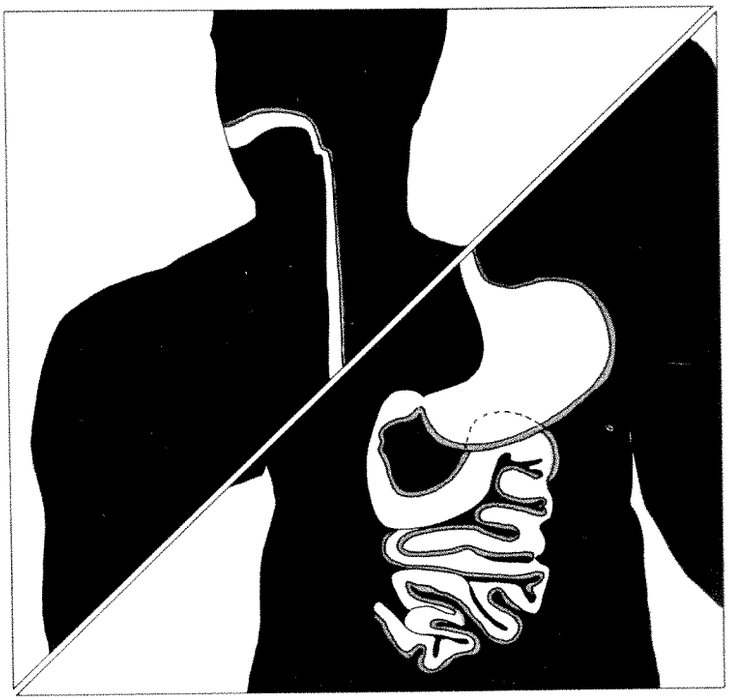
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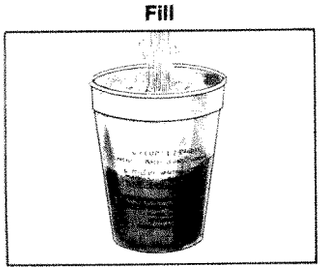
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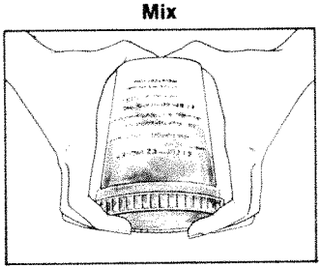
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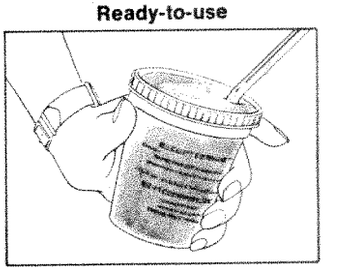
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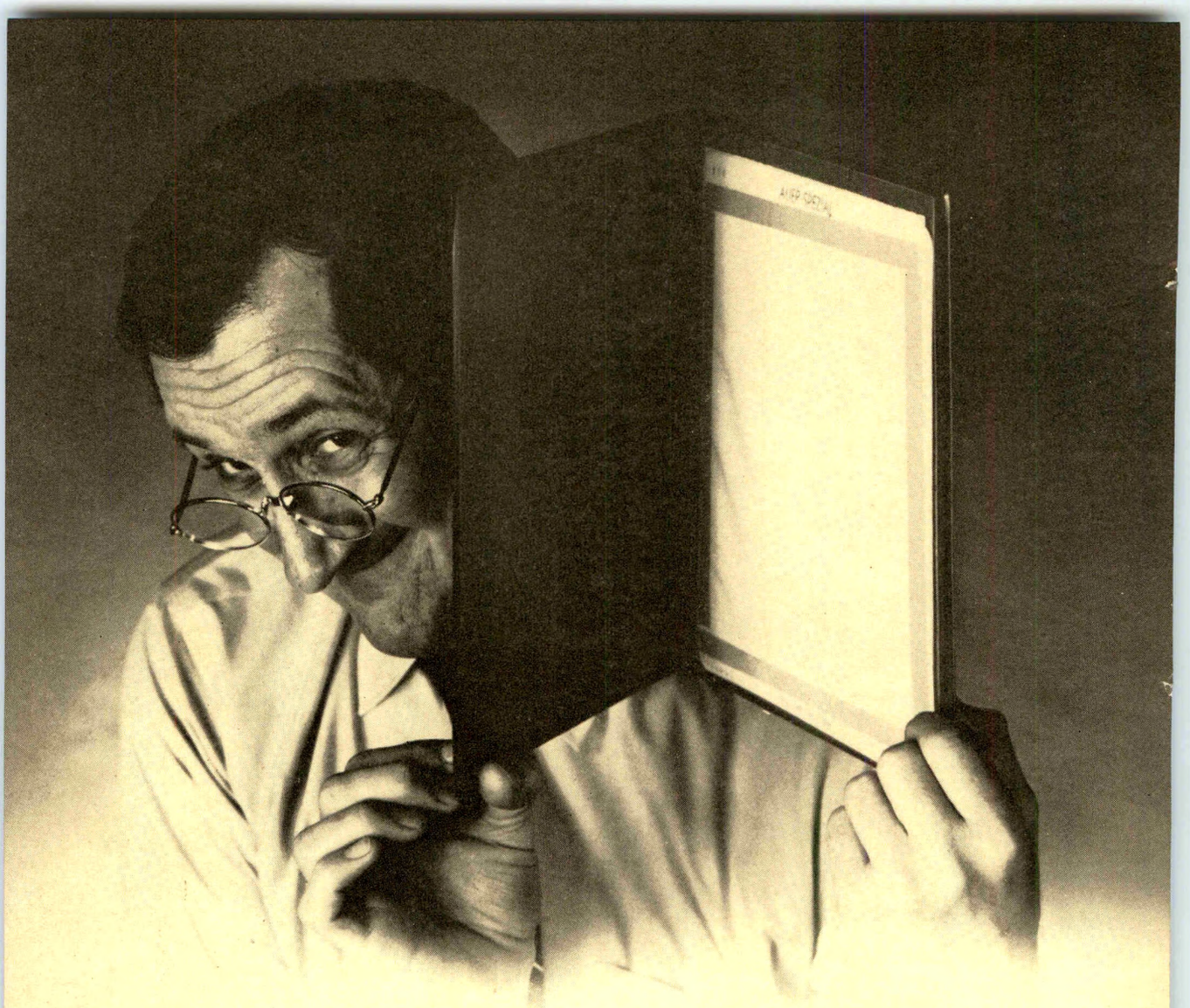
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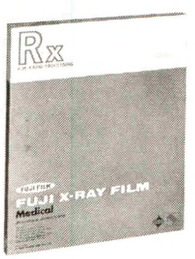
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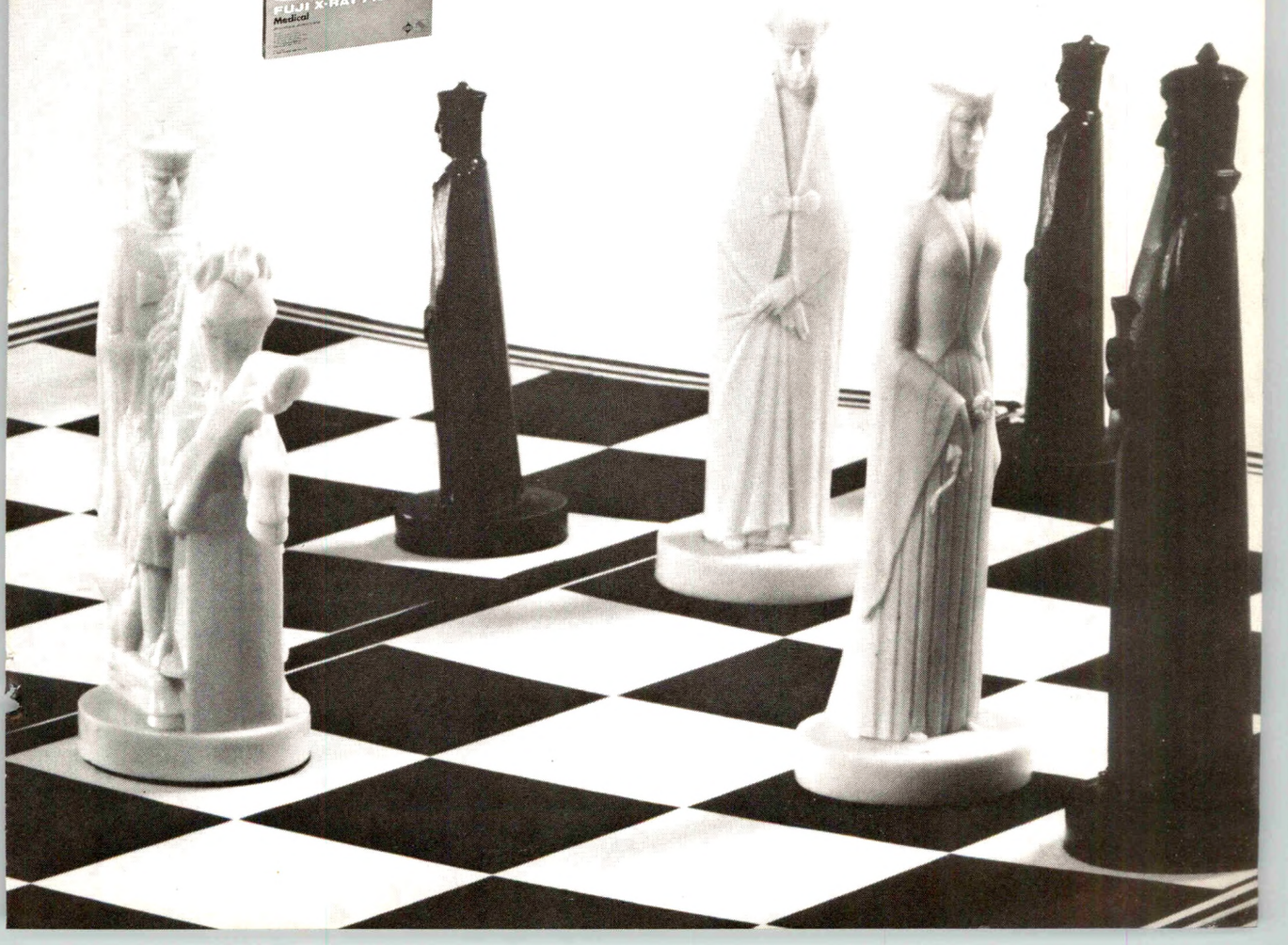
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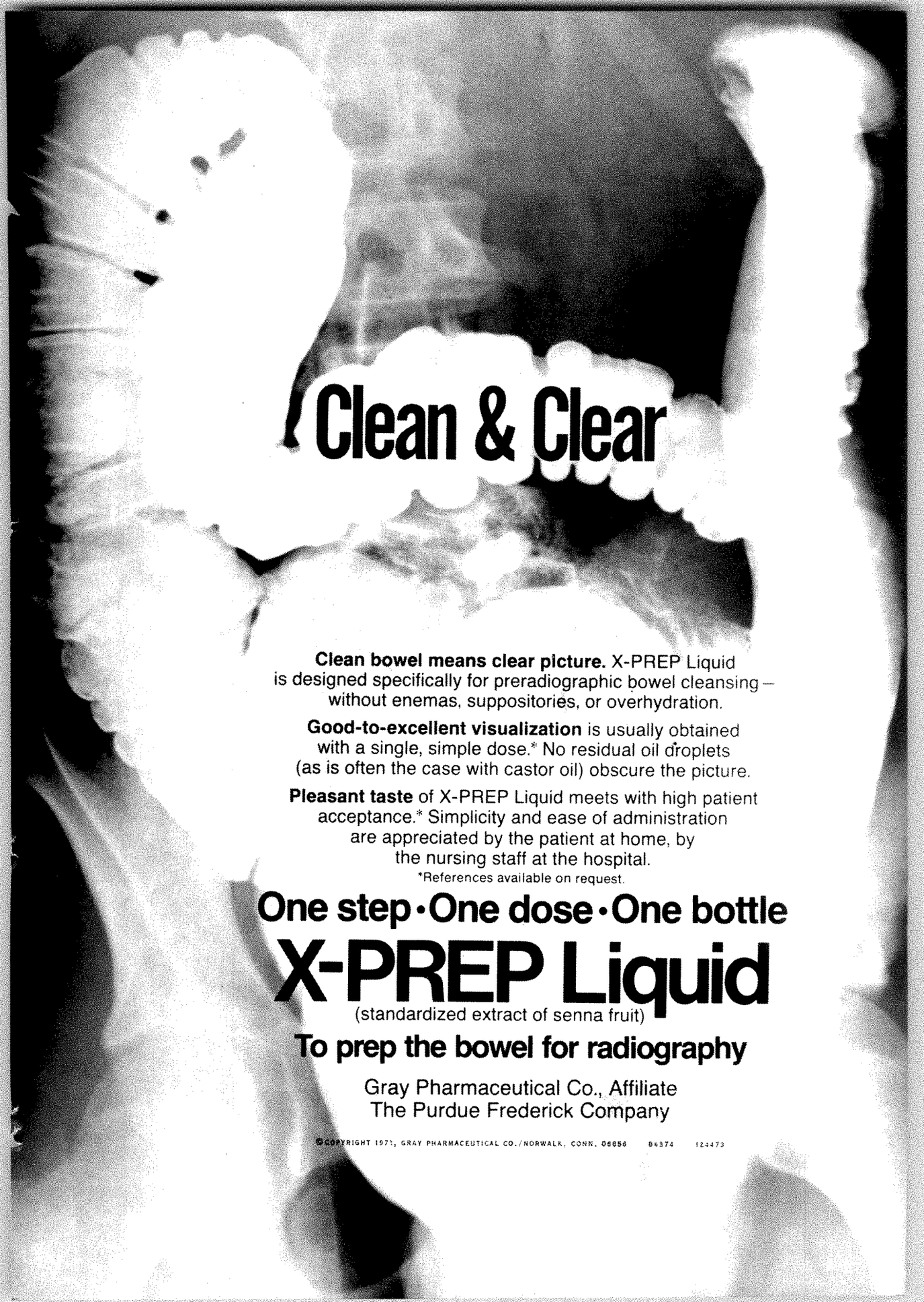
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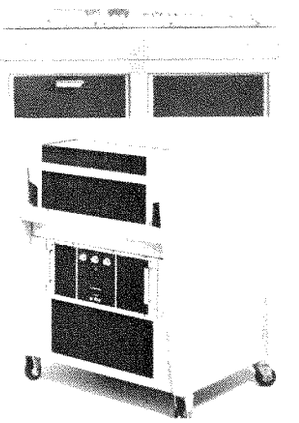
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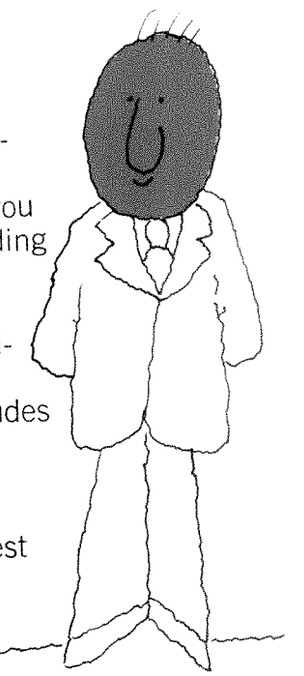
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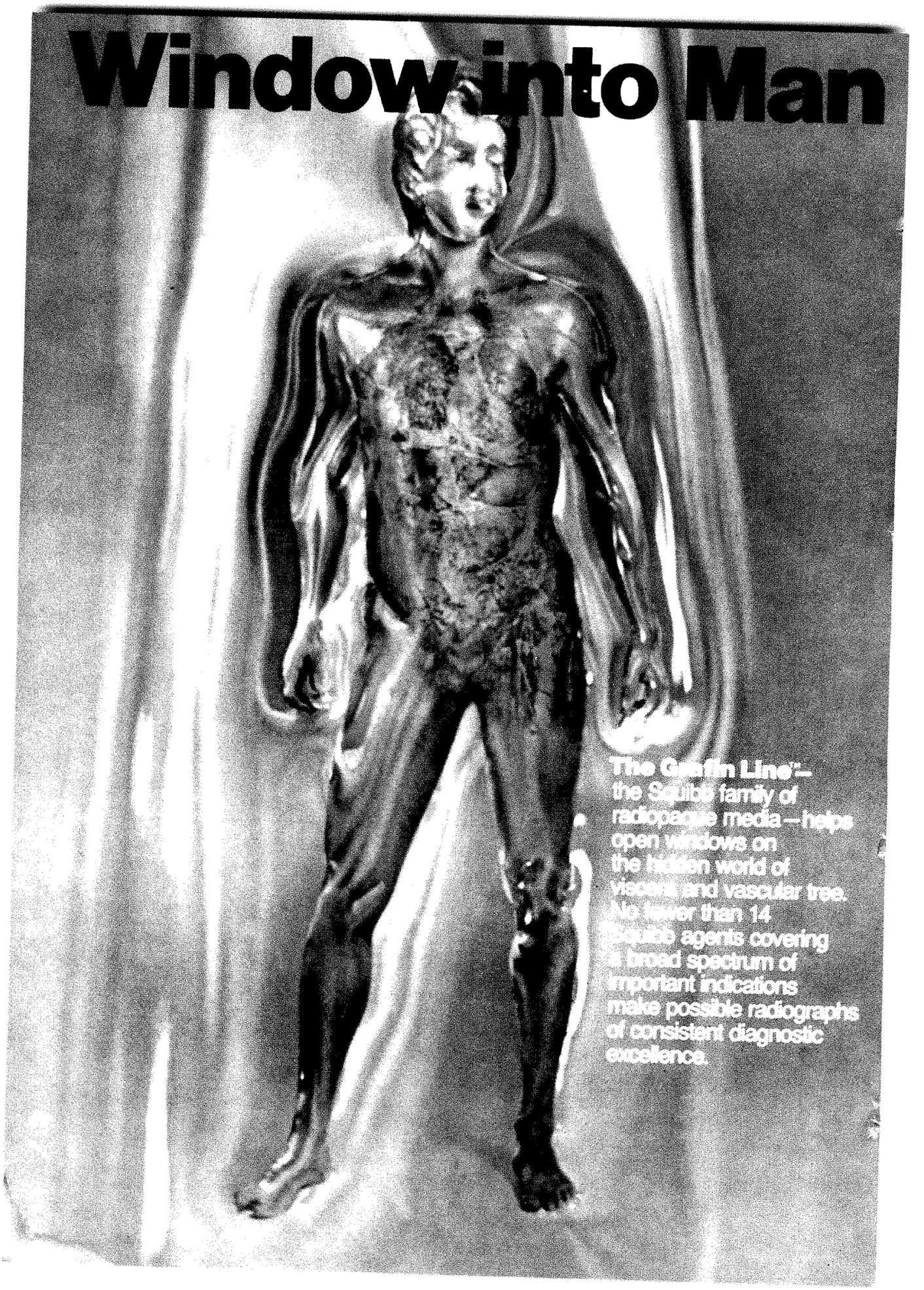
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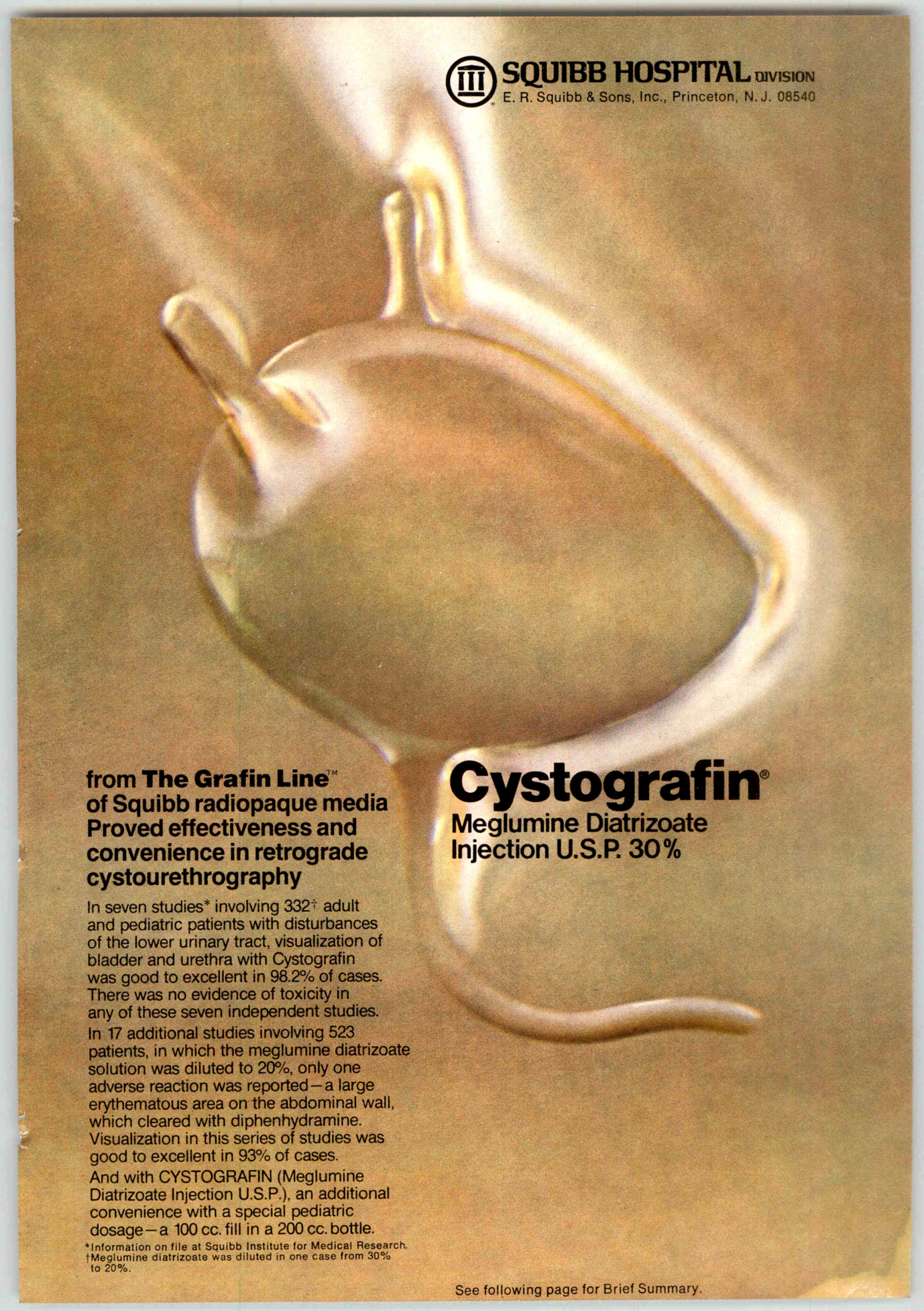


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In seven studies* involving 332† adult and pediatric patients with disturbances of the lower urinary tract, visualization of bladder and urethra with Cystografin was good to excellent in 98.2% of cases. There was no evidence of toxicity in any of these seven independent studies.
In 17 additional studies involving 523 patients, in which the meglumine diatrizoate solution was diluted to 20%, only one adverse reaction was reported—a large erythematous area on the abdominal wall, which cleared with diphenhydramine. Visualization in this series of studies was good to excellent in 93% of cases.
And with CYSTOGRAFIN (Meglumine Diatrizoate Injection U.S.P.), an additional convenience with a special pediatric dosage—a 100 cc. fill in a 200 cc. bottle.
*Information on file at Squibb Institute for Medical Research.
†Meglumine diatrizoate was diluted in one case from 30% to 20%.
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Injection U.S.P. 30%
See following page for Brief Summary.

BRIEF SUMMARY

Cystografin (Meglumine Diatrizoate Injection U.S.P.) provides a sterile, aqueous solution of 30% meglumine diatrizoate containing approximately 14% (42.3 Gm./300 cc.) bound iodine; also containing 0.04% EDTA as a sequestering agent. The preparation is **not intended for intravascular injection.**

Contraindications: In patients with a hypersensitivity to salts of diatrizoic acid.

Warnings: Severe sensitivity reactions are more likely in patients with a personal or family history of bronchial asthma, significant allergies, previous reactions to contrast agents. Use with extreme caution in persons with a history of sensitivity to iodine. *Usage in Pregnancy*—Safety of meglumine diatrizoate for use during pregnancy has not been established.

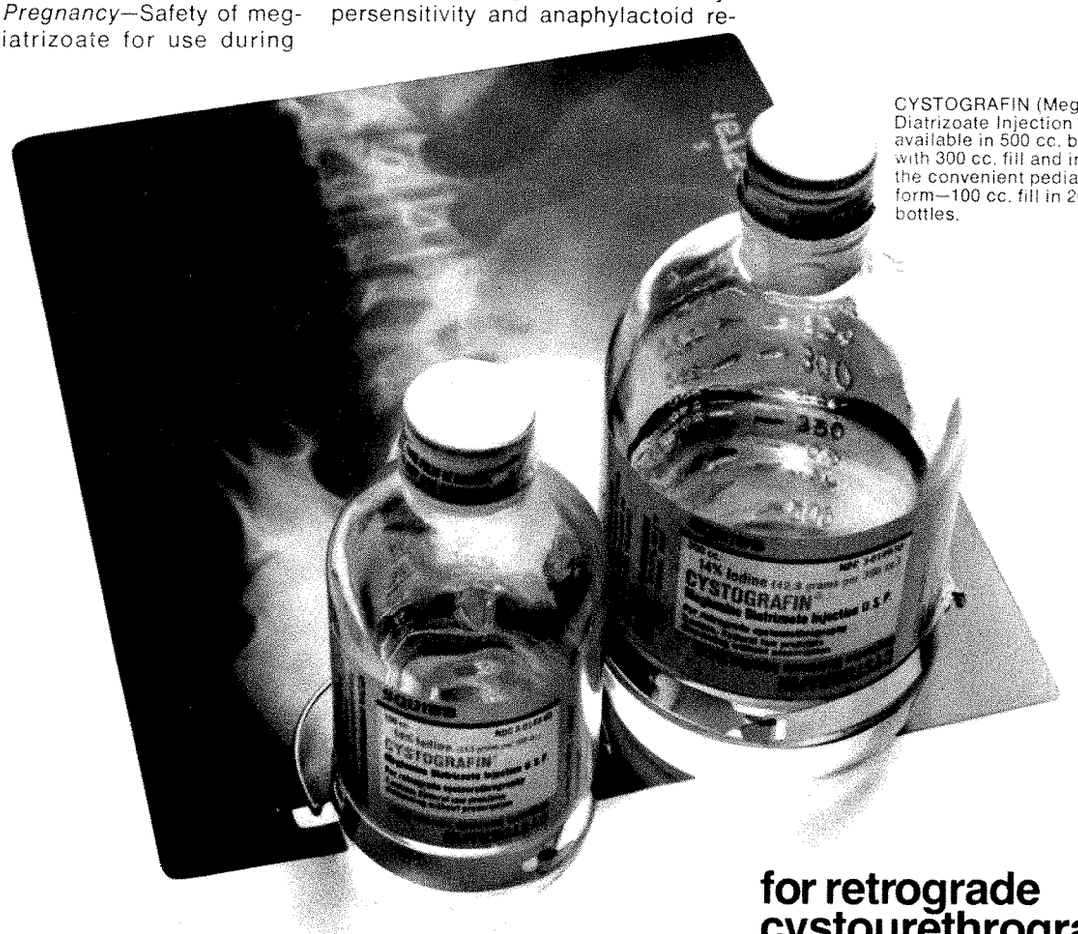
Precautions: Safe and effective use depends upon proper dosage, correct technique, adequate precautions, readiness for emergencies. Perform retrograde cystourethrography with caution if known, active infectious process of urinary tract exists. Use sterile technique during administration and avoid excessive pressure, rapid or acute bladder distention, and trauma.

Adverse Reactions: Hematuria, perforation of the urethra or bladder, introduction of genitourinary tract infection, and oliguria or anuria are complications of retrograde genitourinary tract procedures. Reactions associated with I.V. administration may occur if drug is intravasated; hypersensitivity and anaphylactoid reactions may occur. Severe reactions, which may be manifested by edema of the face and glottis, respiratory distress, convulsions, or shock, may prove fatal unless promptly controlled by emergency measures—clear airway maintenance, immediate use of oxygen and resuscitative drugs.

For full information, consult package insert.

How Supplied: 200 cc. and 500 cc. bottles containing 100 cc. and 300 cc. of meglumine diatrizoate, respectively, with sufficient capacity for dilution up to 167 cc. and 500 cc., respectively.

SQUIBB HOSPITAL DIVISION
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CYSTOGRAFIN (Meglumine Diatrizoate Injection U.S.P.) is available in 500 cc. bottles with 300 cc. fill and in the convenient pediatric form—100 cc. fill in 200 cc. bottles.

for retrograde cystourethrography

- ☐ highly effective visualization of bladder and urethra
- ☐ well tolerated by patients
- ☐ good local tissue tolerance

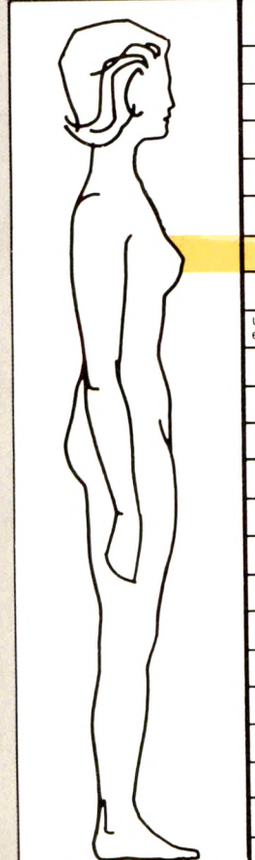
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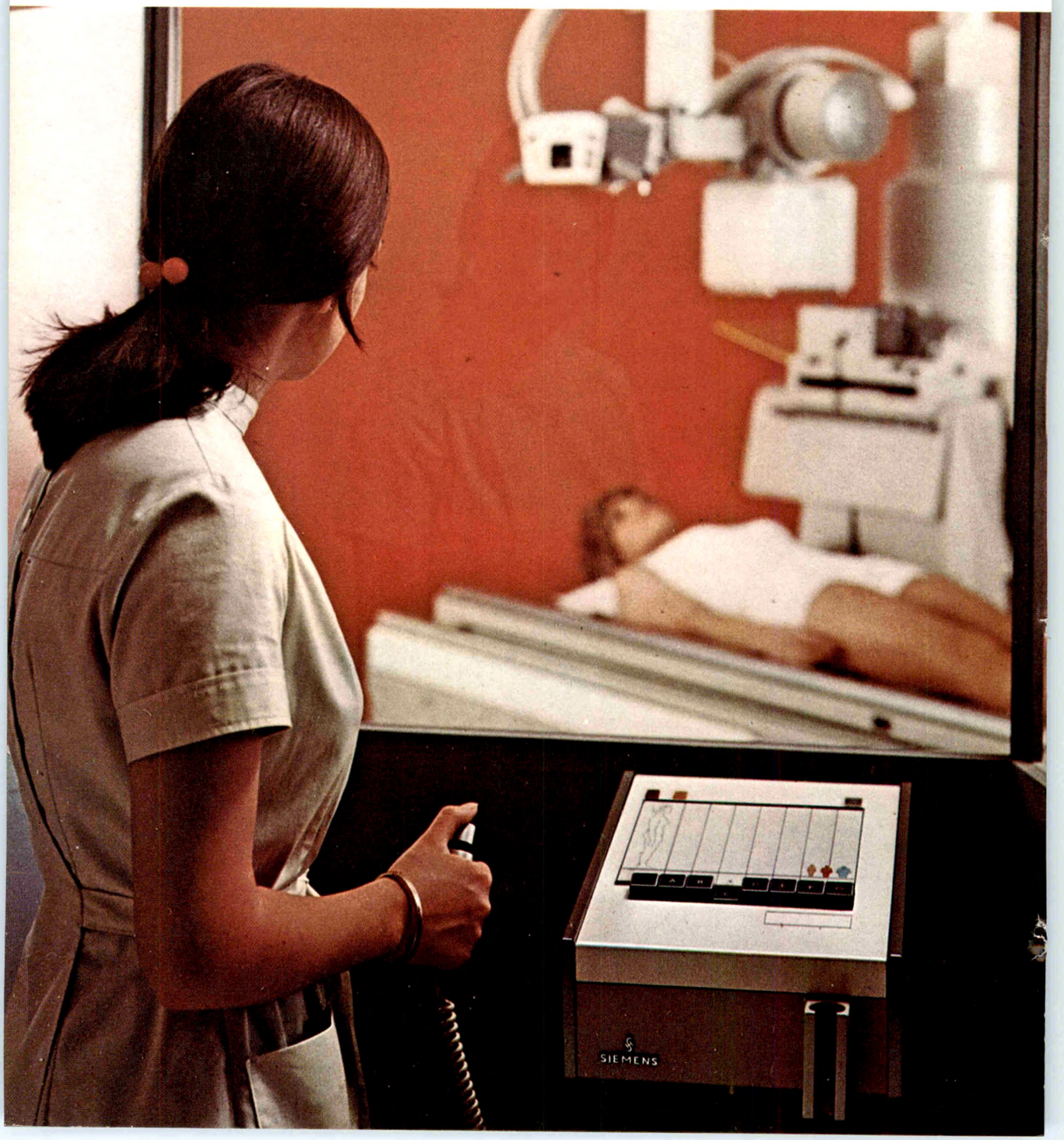
Meglumine Diatrizoate Injection U.S.P. 30%

Siemens presents a systems-approach to radiology.



	A	B	C	D	E	F	G
		cervical column			skull		
		claviculum					
		scapula					
				thoracic column, a.p.	ribs 1-7		
					ribs 8-12		
upper extremity							
	gall bladder	kidney		lumbar column, a.p.		lumbar column, lat.	
				pelvis			
	urinary bladder neck of femur			sacrum and coccyx, a.p.		sacrum and coccyx, lat.	
	femur						
lower extremity							
kV	50	60	60	73	73	81	
screen	high speed	high speed	high speed	high speed	detail	high speed	
focus	■	■	■	■	▣	■	▣
measuring field	▖▗	▖▗	▖▗	▖▗	▖▗	▖▗	▖▗

Siemens Tridoros Optimatic. A multi-unit system with individual local unit consoles.



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Siemens now offers a way to expand radiological facilities while at the same time optimizing the use of equipment and key personnel.

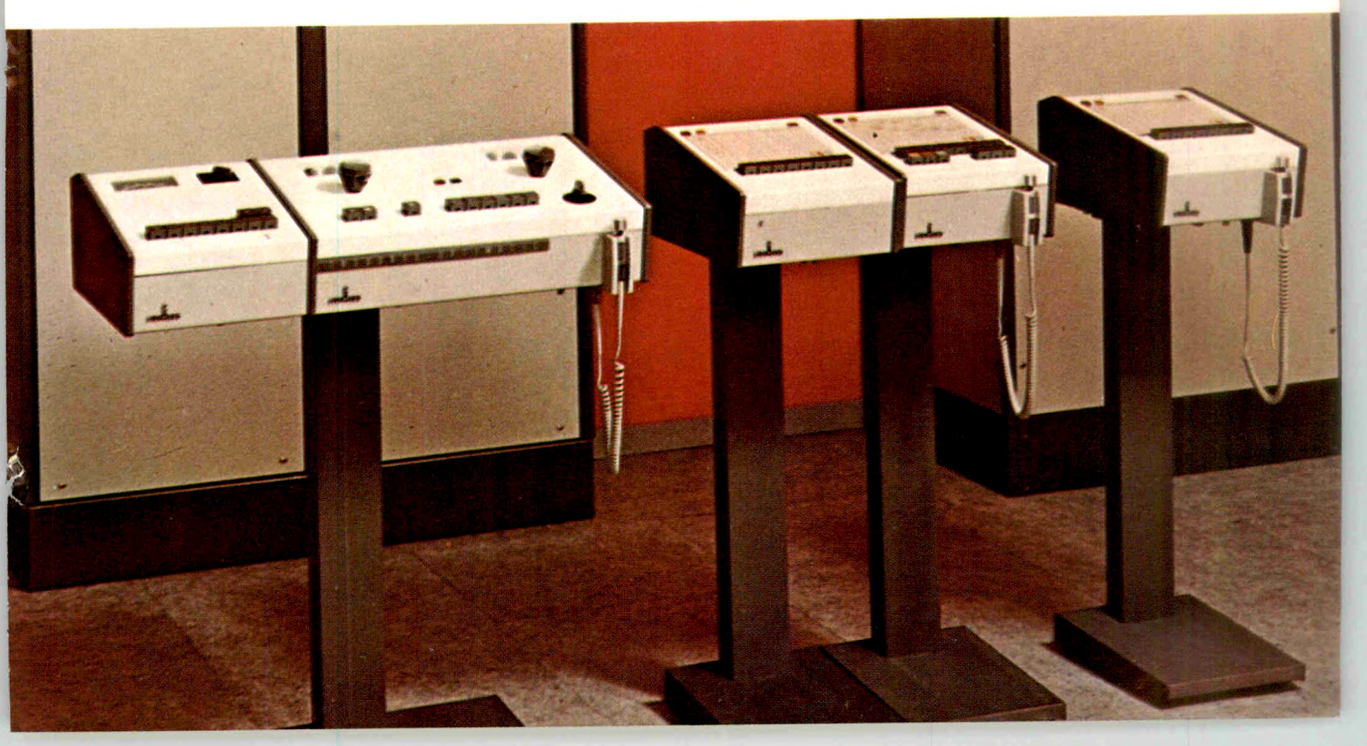
The Tridoros Optimatic system consists of a single centrally located, time-shared master generator with an analog computer and three or more pushbutton operated local consoles.

A new Tridoros Optimatic installation with four examination units usually costs considerably less than a similar setup using individual generators. But the major advantage of the new system is in the way it cuts to a minimum the number of decisions and adjustments the operator has to make to get optimum results.

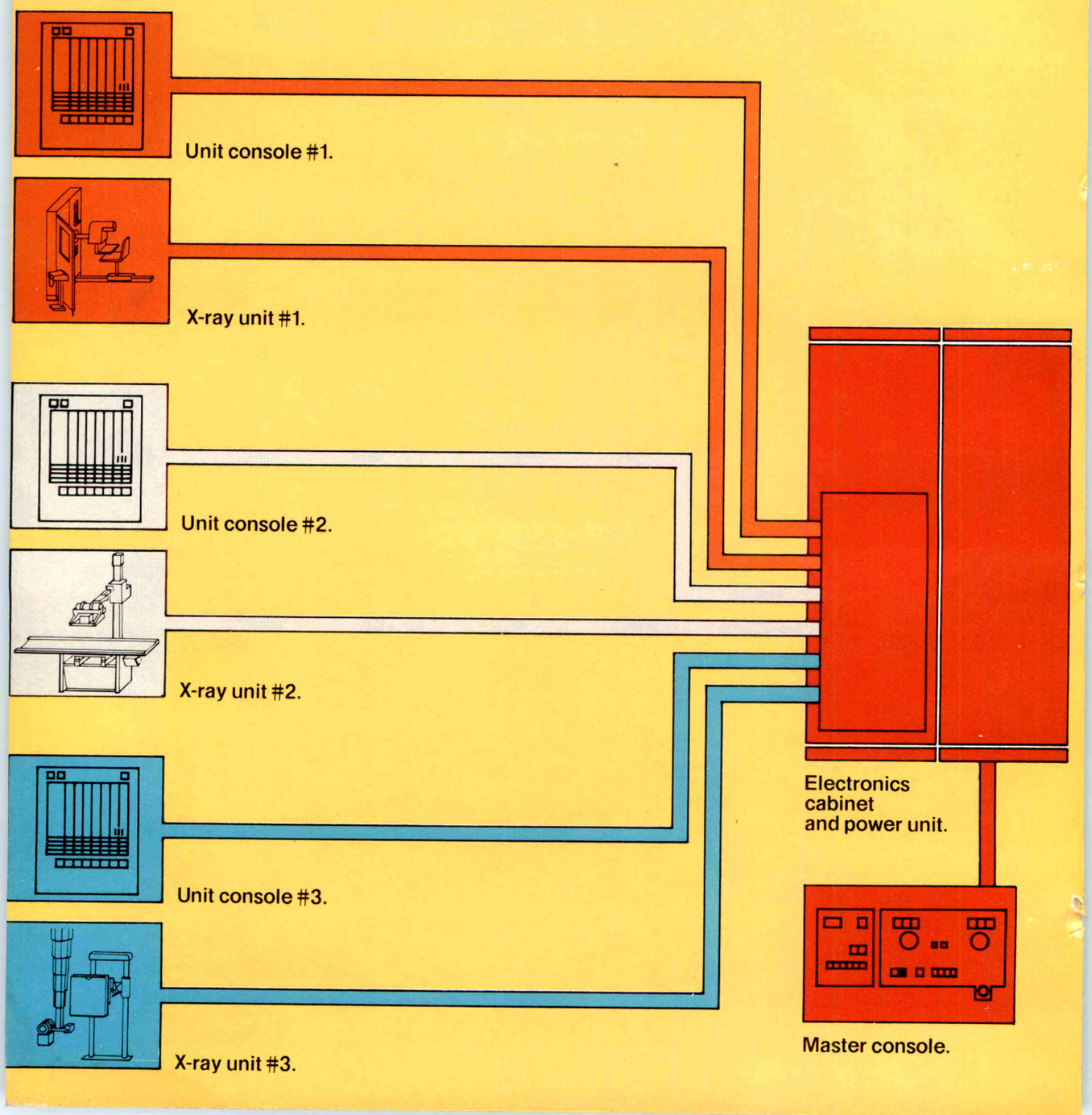
Technicians can now handle a much greater patient load while producing consistently superior radiographs.

At left: Technician starts automatically timed exposure at unit using overtable tube.

Below: Elements of the Tridoros Optimatic system including electronics cabinet (left rear), power unit (right rear) and left to right, master console and three unit consoles.



Consoles are "human-engineered" to provide organ-related pushbutton exposure control.



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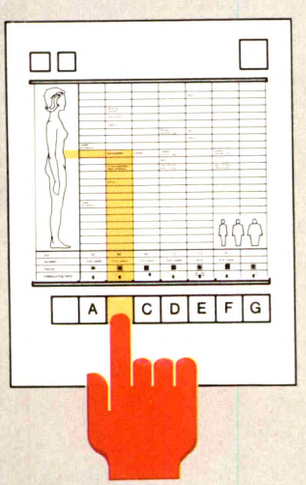
A Tridoros Optimatic unit console is set up in the immediate vicinity of each examination unit so that technicians are close to their patients.

To set the exposure at one of the consoles, the technician pushes one of the seven organ-related buttons. This automatically selects the kV, focal spot, screen combination and film blackening needed for the particular type of exposure to be made.

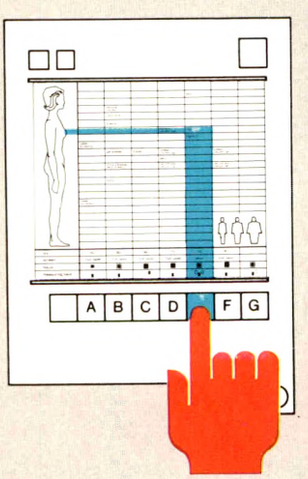
These unit console panels have a number of important advantages. They make data selection simpler than ever before. They greatly reduce the possibility of errors. And they assure consistently high quality radiographs.

At left: A Tridoros Optimatic setup consisting of three examination units with their individual consoles. Any unit can also be operated from the master console at lower right.

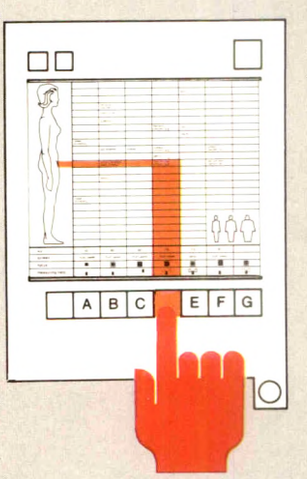
Below: Technician prepares for exposure by pushing desired organ-related button.



Pushbutton "B" sets typical Bucky table program for gall bladder, thin patient: 60kV, high-speed screen, small focal spot, Iontomat* center chamber.



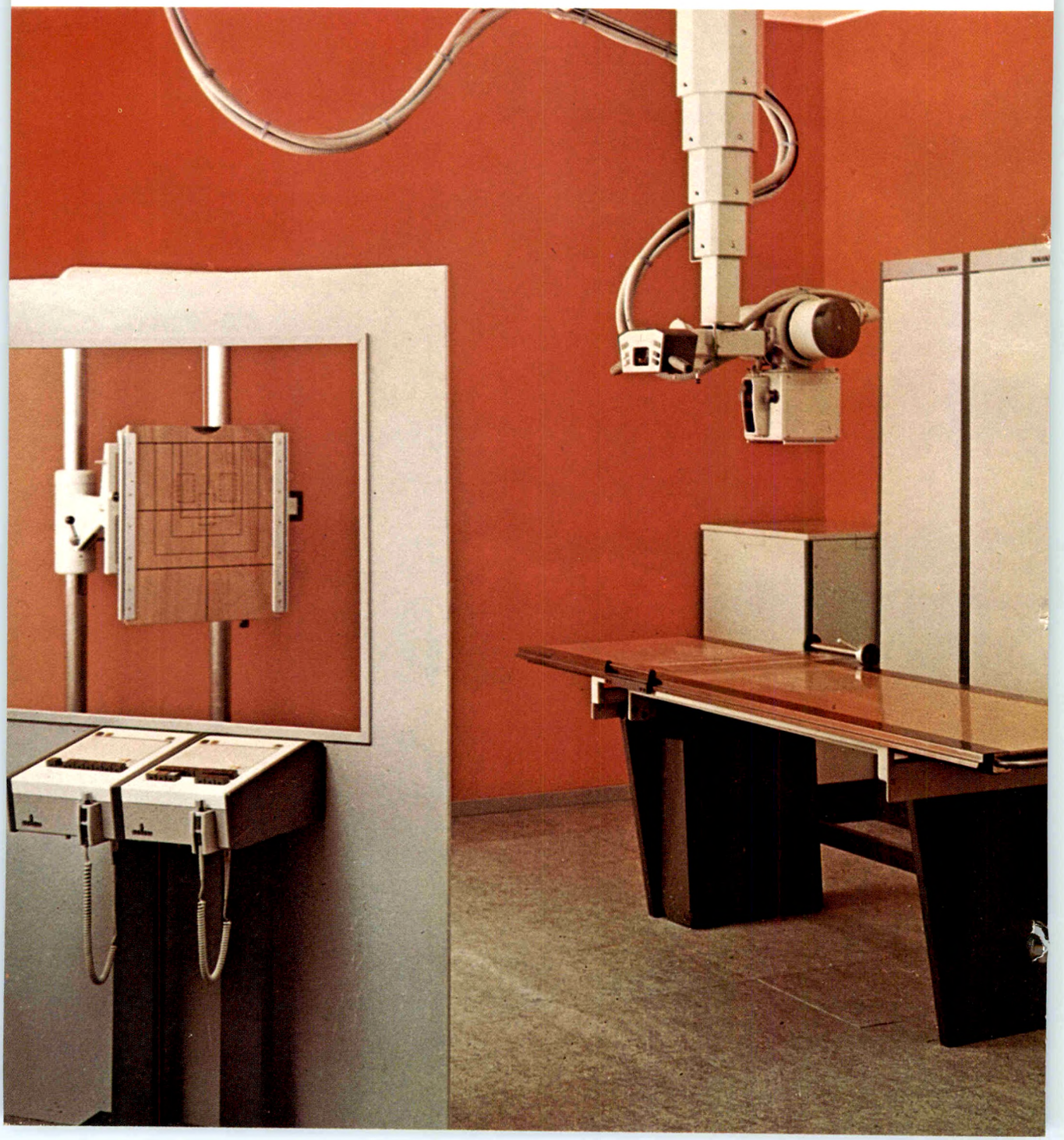
Pushbutton "E" sets typical Bucky table program for ribs 1-7, medium patient: 73kV, detail screen, small focal spot, Iontomat* center chamber.



Pushbutton "D" sets typical Bucky table program for sacrum and coccyx a.p., heavy patient: 73kV, high-speed screen, large focal spot, Iontomat* center chamber.

*Ionization chamber.

Now x-ray department layouts can be planned for optimum use of available space.



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In many cases, where x-ray units are operated centrally from a console, compromises in the positioning of both the console and the examination units is necessary.

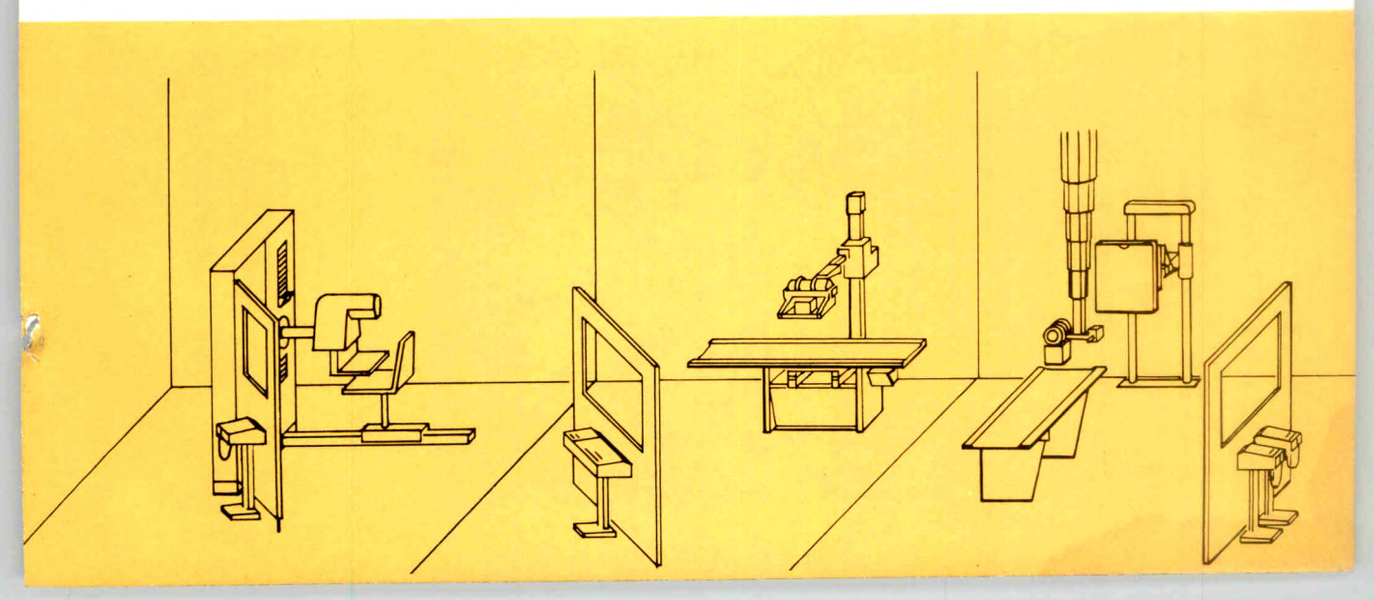
With the unit consoles of the Tridoros Optimatic system, the lay-out can be arranged in a more flexible manner.

In the setups shown below, technicians can preset pushbuttons either before or after positioning the patients. The actuated pushbuttons do not interfere with operation of other units. Only during the brief interval when an actual exposure is being made at one console is the use of the generator blocked for the other consoles. These exposure intervals are visually displayed by means of indicator lights on each console.

The new Siemens system permits the complete decentralization of any or all x-ray equipment. This is a significant advantage when an old installation is being modernized.

At left: Bucky wall stand and Bucky table with paired unit consoles.

Below: Four consoles are set up near the units they control. With this kind of arrangement and the automated exposure of the Siemens system, technicians can concentrate on patient positioning.

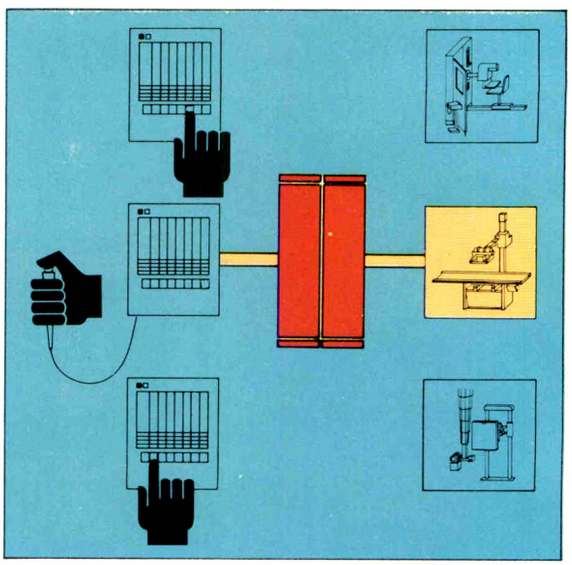


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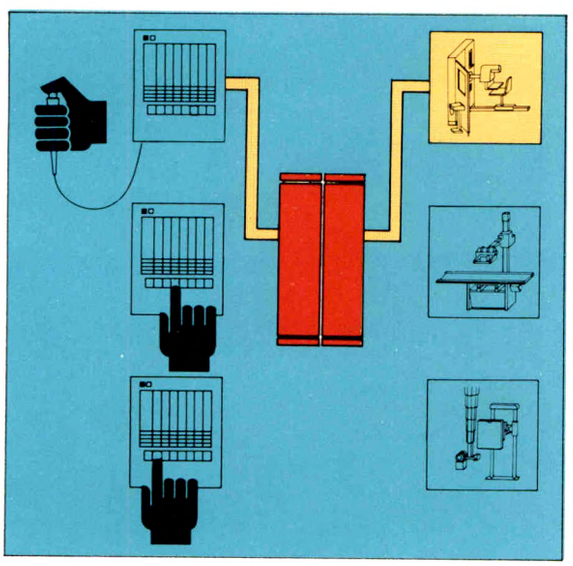
A new, practical way to improve the capability of your x-ray installation.

The Siemens Tridoros Optimatic system cuts to a minimum the number of decisions and adjustments technicians must make to get optimum results. Data selection and timing of all radiographic exposures are completely automated. And organ-related programs can be set simultaneously on several units.

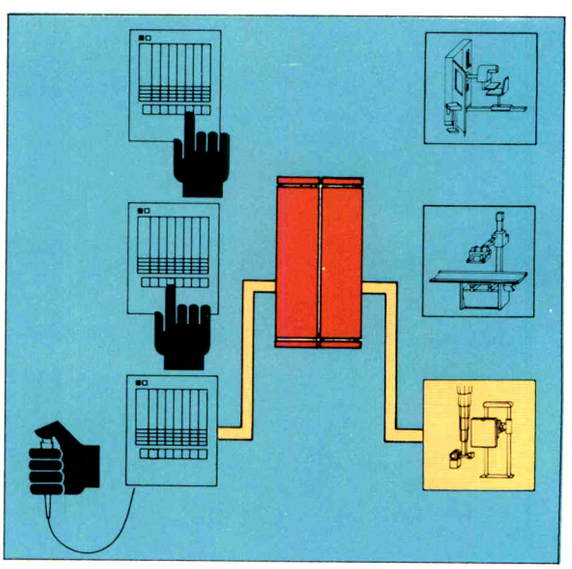
The preceding pages will give you an idea of how this new Siemens system can help you make the most efficient use of your radiological equipment and personnel. If you'd like to know more, please write Siemens Corporation, Medical Systems Division, 186 Wood Avenue South, Iselin, N.J. 08830.



(2) Programs for mammography and Bucky wall unit are selected while planigraphic exposure is made at unit console.



(1) Exposure is triggered for mammography while programs are selected at planigraphic table and Bucky wall stand.



(3) Third exposure is made at unit console controlling Bucky wall stand as programs are selected for the other two radiographic units.



Hysterosalpingogram with Salpix Contrast Medium.



24-hour postinjection x-ray of same patient.

now you see it

now you don't

With Salpix as your contrast medium, your gynecologic patient needn't undergo the 24-hour postinjection x-ray usually required with iodized oils. Water-soluble Salpix leaves virtually no irritating radiopaque residue to produce foreign-body reactions, yet it provides the viscosity needed for adequate visualization.

Contraindications: Contraindications to hysterosalpingography include the presence of severe vaginal or cervical infections, existing or recent pelvic infection, marked cervical erosion or endocervicitis, and pregnancy. The procedure is contraindicated during the immediate pre- or post-menstrual phase.

Sensitivity Test: If indicated in the patient's history, an intracutaneous skin test or sublingual absorption observation may be done with 0.1 cc Salpix.

Warning: Not for intravenous use.

© ORTHO PHARMACEUTICAL CORPORATION 1970

CONTRAST MEDIUM

Salpix

TRADEMARK

EACH CC CONTAINS:
sodium acetrizoate 0.53 g and
polyvinylpyrrolidone 0.23 g

Ortho

ORTHO PHARMACEUTICAL CORPORATION • RARITAN, NEW JERSEY 08869



One if by land... two if by sea... three if by Profexray.

The breakthrough is coming.

Here's the leader of things to come in radiology equipment: third-generation design in x-ray generators.

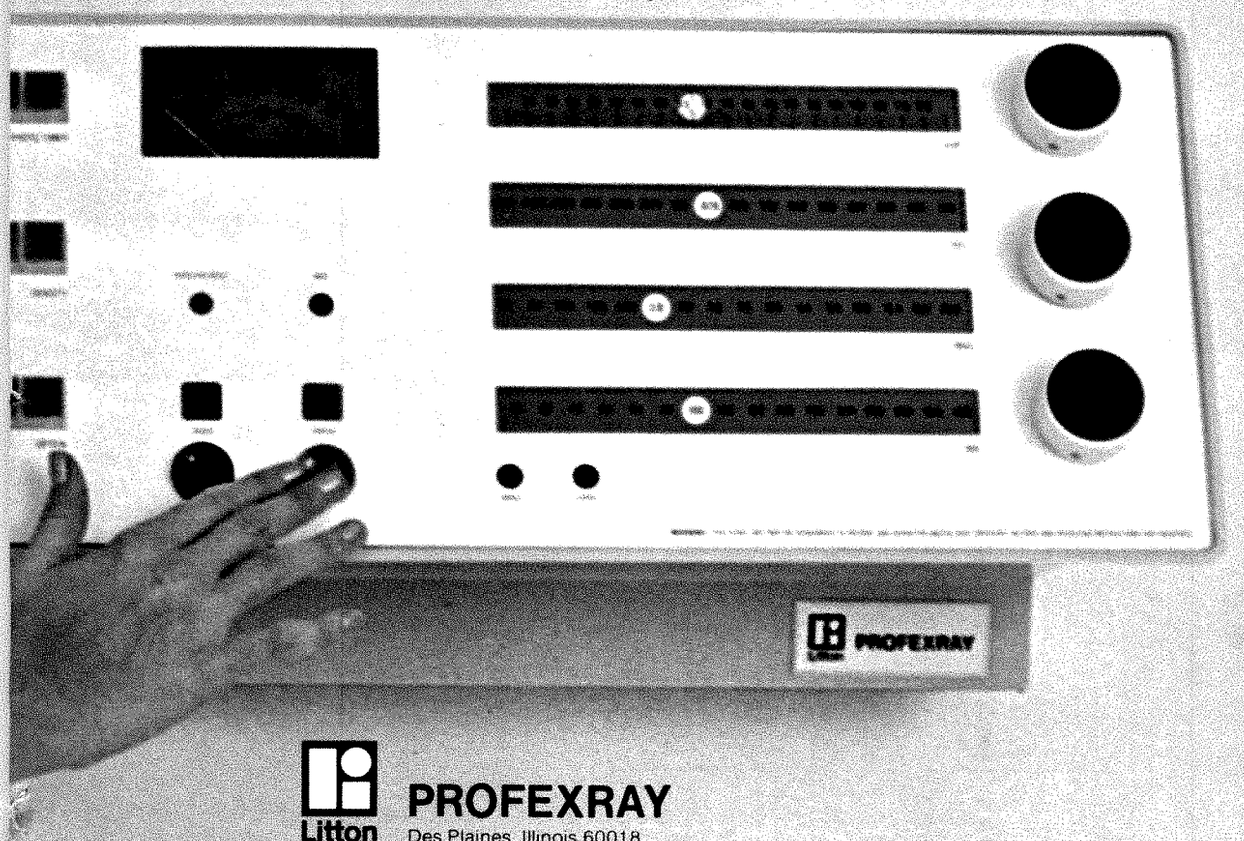
It's the Profexray Patriot. The first of a new line of totally modular, three-phase generators. It's your opportunity to initiate three-phase capability at a single-phase price. It's our opportunity to revolutionize the way you expose x-ray film.

The new Patriot generator delivers 800 mA, 125 KV. Its control panel is completely detachable; you can leave it on top of the compact, desk-height generator. Or you can install it in a remote-control console. Or you can simply hang it on a wall—in the radiology department, in an operating room—*anywhere*.

The Patriot three-phase generator is a major American technological accomplishment. It is only one of many new Profexray units, each built to a key concept that will speed a procedure, overthrow an outmoded way of doing things, innovate changes that can *revolutionize* your departmental efficiency.

You really ought to talk to your Profexray man.

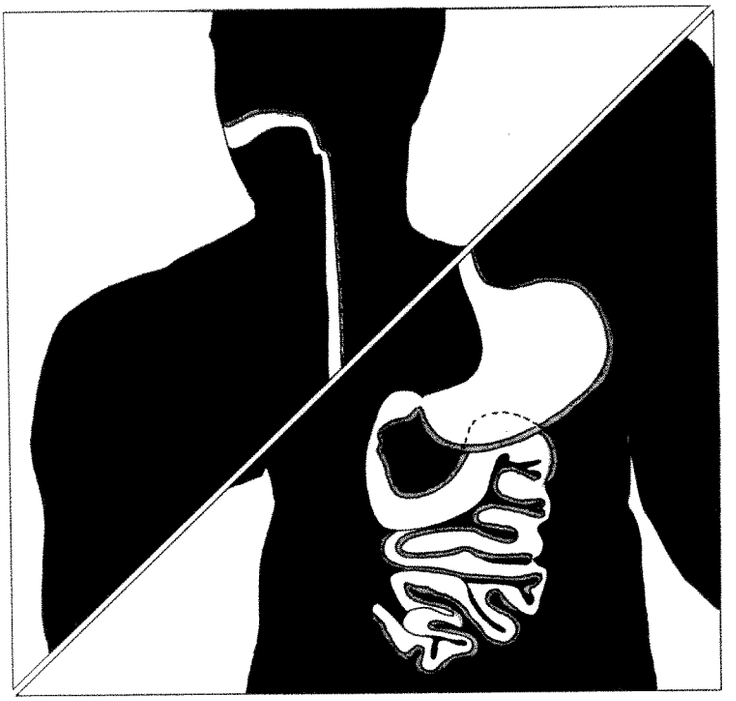
Ask him about his revolutionary ideas.



Litton **PROFEXRAY**
Des Plaines, Illinois 60018

Litton technology:
The 2nd American Revolution.

It's only half as far...



from start to cecum with E-Z-Paque™

Figuratively speaking it is. Because transit-accelerated E-Z-Paque passes through the small bowel in half the usual time.

The reason is its built-in "chaser".

Since E-Z-Paque was expressly formulated for upper G.I. use, it was formulated with a hydrophilic smoothing agent to make it move through the digestive tract with ease.

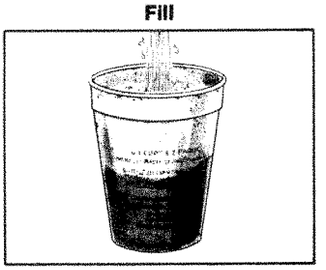
So, without sacrificing opacity, you get continuous flow for a puddling-free diagnostic pattern.

And you can often complete a small bowel series in only 40 minutes' time.

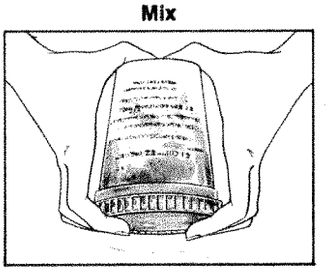
Try transit-accelerated E-Z-Paque for your next upper G.I. examination. For time-savings it's unsurpassed. And for money-savings, too. You can get E-Z-Paque in its unique, spill-proof G.I. Cup for no more than it would cost to measure, pour and mix barium from a bulk container.

E-Z-PAQUE™

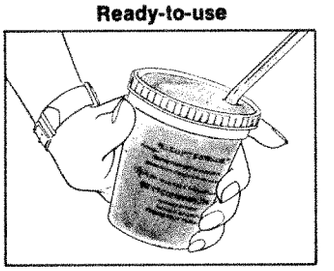
Fill



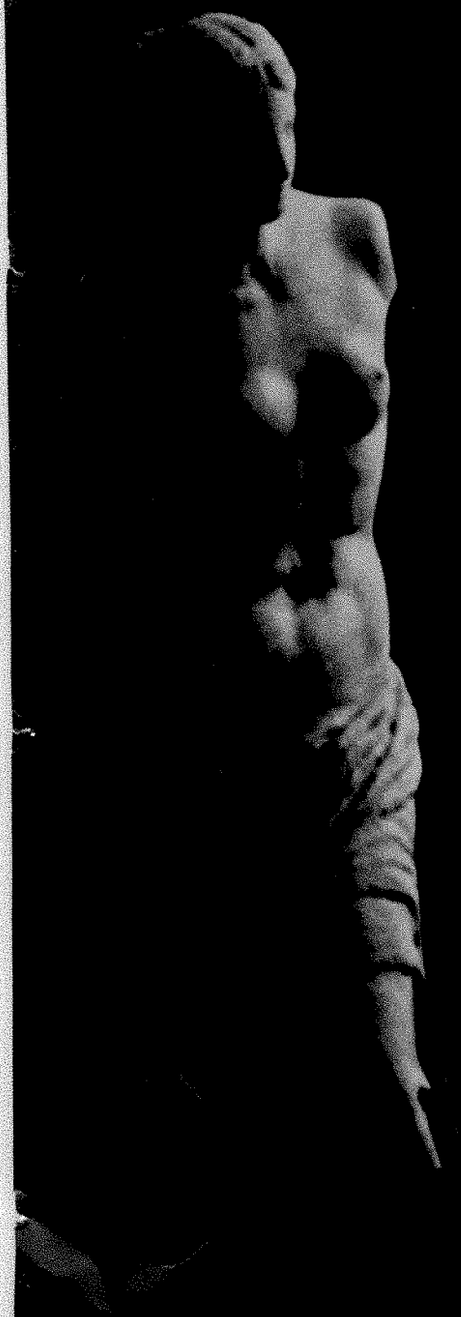
Mix



Ready-to-use



E-Z-EM PIONEERS IN G.I. RADIOLOGIC ACCESSORIES
111 Swalm Street, Westbury, N. Y. 11590 (516) 333-8230



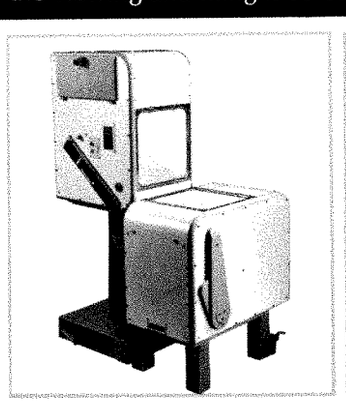
the beauty of the naked film sheet

in SCHONANDER CUTFILM CHANGERS is that...

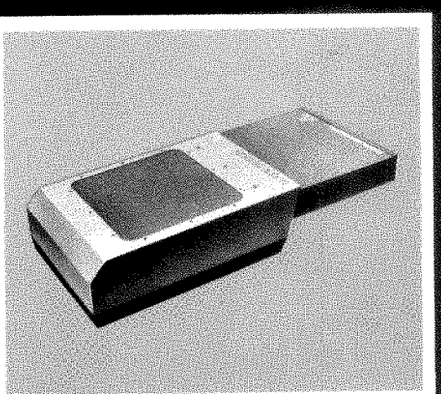
- it has the lowest possible inertia – therefore it can be accelerated and decelerated fast in the machine to give adequate exposure times at all exposure rates, and the changer does not cause disturbing vibrations when it runs;
- it gives excellent detail without vacuum procedures;
- the handling is so simple: just load the unexposed films in the loading bin and pick up the exposed films in the receiver;
- it allows you to take any number of single films without wasting any film;
- it allows preliminary evaluation of the examination without delay by having just a few films processed immediately;
- it allows alternate exposures in biplane operation – for a minimum of scatter – without any film waste;
- unlike rollfilm (cut or uncut) it is initially flat, so it runs smoothly through the processor;
- the viewing and filing is so convenient.

SCHONANDER FILMCHANGERS for naked sheetfilm are

CONVENIENT
ECONOMICAL
DEPENDABLE



AOT-R max. 6 exp./sec.
Universal filmchanger for all angiographic examinations

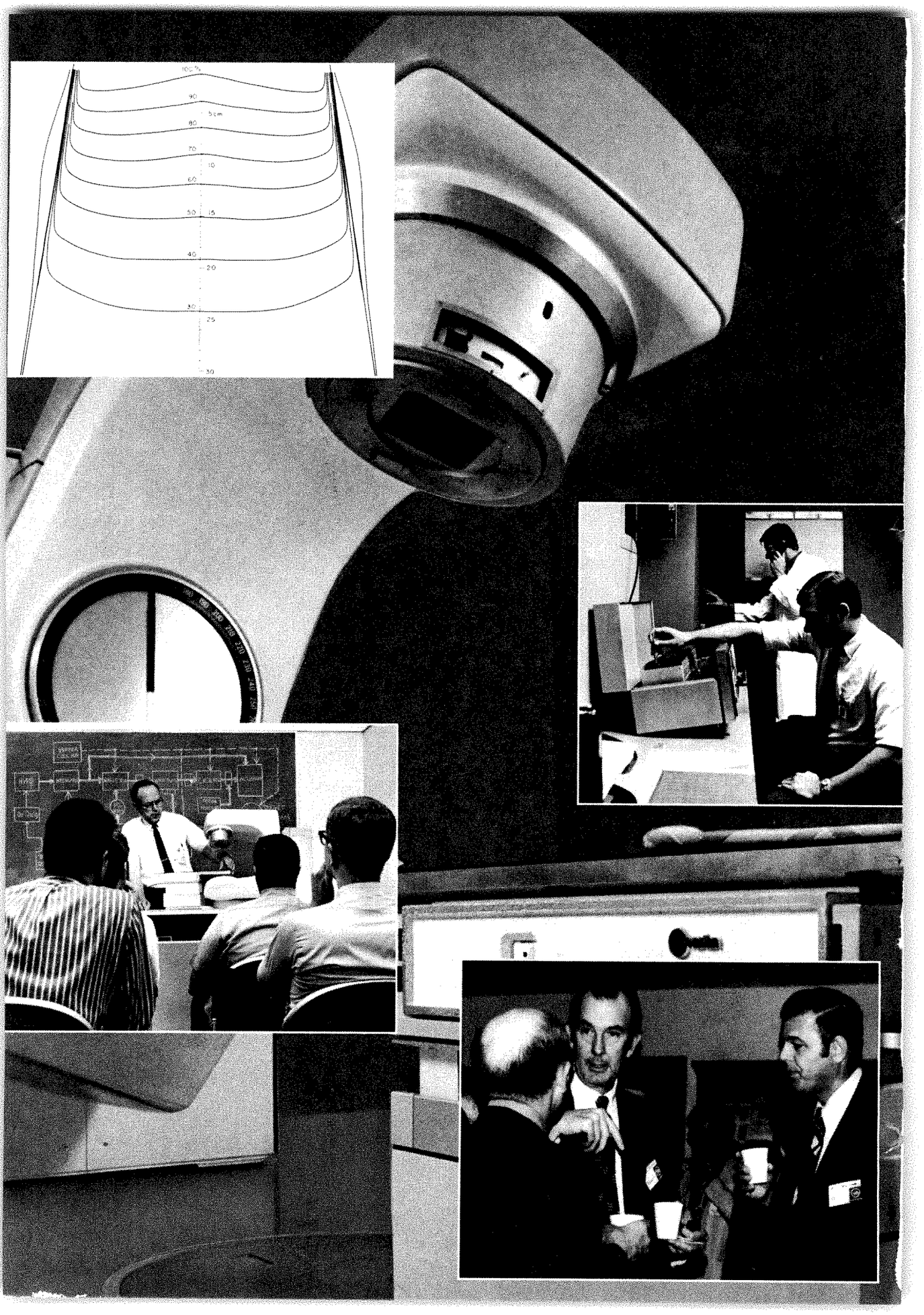


PUCK max. 2 exp./sec.
Punch card controlled filmchanger with see-through options; also useful to replace cassettes in conventional radiography

ELEMA-SCHONANDER

ELEMA-SCHONANDER, INC.

699 LIVELY BOULEVARD ■ ELK GROVE VILLAGE, ILL. 60007 ■ (312) 593-6770


105 %
90
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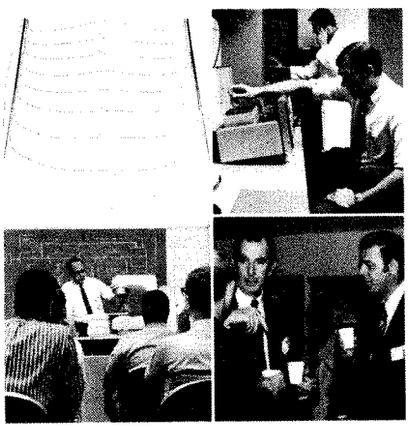
If the Clinac® is so great, why does it take 35 people to help you use it?

We want to be sure every Clinac user gets out of our equipment all the radiotherapy capability we build into it. That's plenty. The versatility, performance and reliability engineered into the Clinac is a matter of record.

So once we had mastered the technical problem, we gave the human element our attention. We set up a specialized customer assistance force which today includes 35 professionals devoted to staff training, technical field assistance and interchange of new data and techniques.

It all starts when your technologist, your maintenance engineer and perhaps you yourself attend a one-week seminar in Palo Alto on operation and maintenance of the Clinac. Using professionally written, illustrated manuals, Varian technicians guide your staff through the theory behind the Clinac, the working components and preventive maintenance techniques. Your people return trained to put your Clinac into operation and perform normal routine maintenance.

After your Clinac goes in service, periodic calls and on-site visits are made to verify its continuing high level performance.



These contacts may lead to service tips, retrofit of a latest innovation, sharing of information about new data available or new accessories under development. If a knotty service problem develops, a close-by Varian field technician is available on 24 hour call.

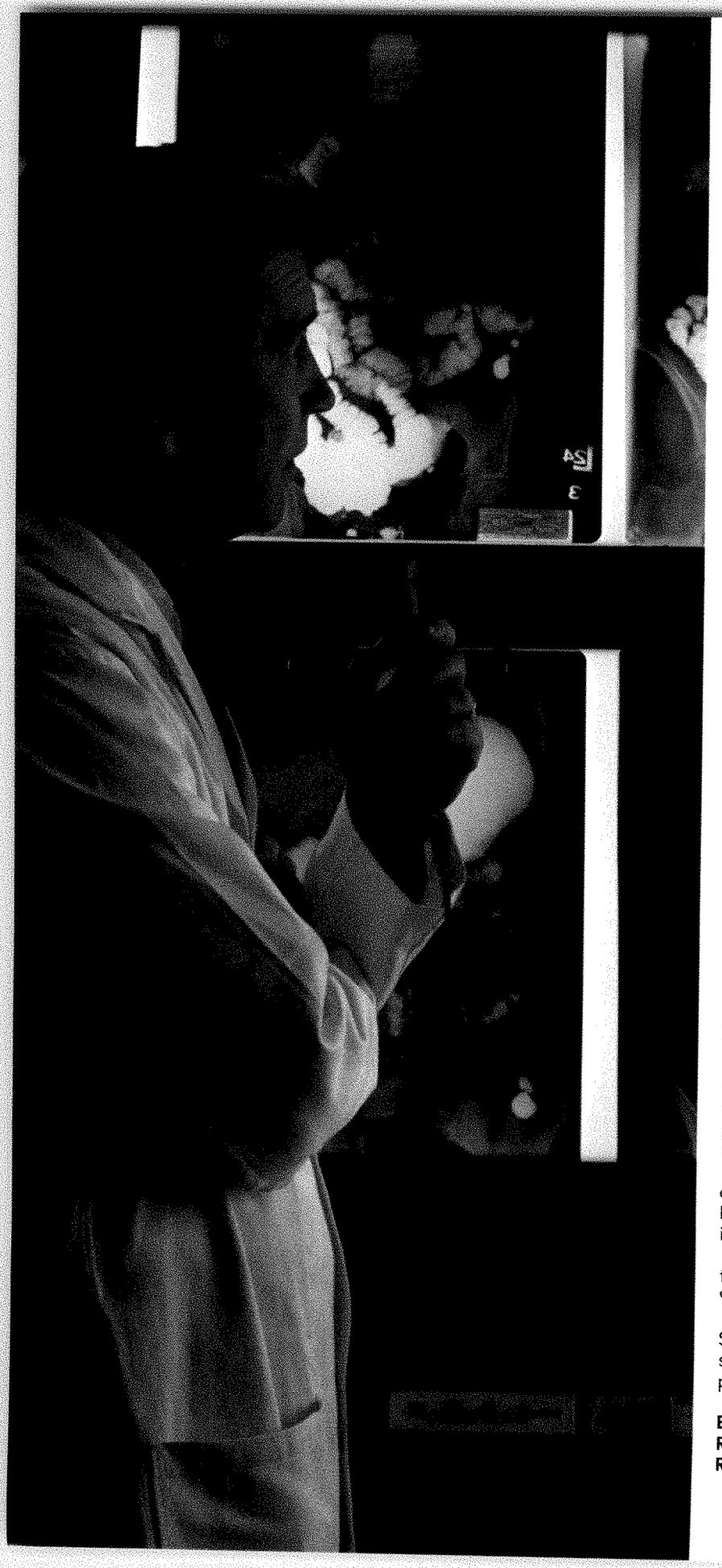
In addition, you will be invited to attend and participate in periodic Varian Users' Meetings. These meetings, which have been attended by as many as 125 therapists and physicists, are a forum for exchange of new data and techniques on the Clinacs.

At the last meeting, held at Geisinger Medical Center, the complete sets of isodose curves, as developed and checked by several leading institutions, were intercompared, and the uniformity of machines verified. User developed tables of tissue-air ratios and scatter-air ratios were distributed. The use of special accessories was discussed, and techniques of using the Clinac in unusual therapy situations were presented. In addition to the formal presentations, you will often learn useful tips on technique from informal discussions with other users and with Varian engineers.

Think about it. Isn't this the type of on-going support you want for the linear accelerator you buy. Call or write for all the details.

Varian Radiation Division, 611 Hansen Way, Palo Alto, California, (415) 493-4000; Springfield, New Jersey, (201) 376-6632; Detroit (Plymouth), Michigan, (313) 455-1570; Chicago (Park Ridge), Illinois, (312) 825-6232; Atlanta, Georgia, (404) 761-3109. In Europe: Steinhauserstrasse, 6300 Zug, Switzerland; Russell House, Molesey Road, Walton-on-Thames, Surrey, England. In South America: Alameda Lorena, 1834 ZC 5 Cerqueira Cesar, Sao Paulo—SP—Brazil.

varian
radiation division



Our commitment to quality—and to you—is one of the reasons you can have confidence that the Kodak x-ray film you use will do the job you want it to do. And do it well.

And you can have equal confidence that the x-ray film you need for your diagnostic program is available from Kodak, because we give you a broad range to choose from—each film designed for a specific medical radiographic requirement.

In cases where reduced exposure is essential, your best choice is KODAK *RP* ROYAL X-OMAT Medical X-ray Film—the fastest *RP* X-OMAT Film we make. It combines speed with high contrast to give you the detailed diagnostic information you want.

And in cases where the subject contrast imparted by bone, air, or contrast media needs enhancement to provide maximum diagnostic detail, we recommend KODAK *RP* X-OMAT Medical X-ray Film.

We also give you a choice of special-application films—for mammography, subtraction, duplicating, photofluorography, and therapy localization procedures.

And now, we are extending your choice with the new KODAK X-OMATIC Films—a totally new approach to improved image quality.

All of these films give you the timesaving advantages of automatic 90-second processing.

Contact your Kodak Technical Sales Representative for a demonstration or consult your medical x-ray products dealer.

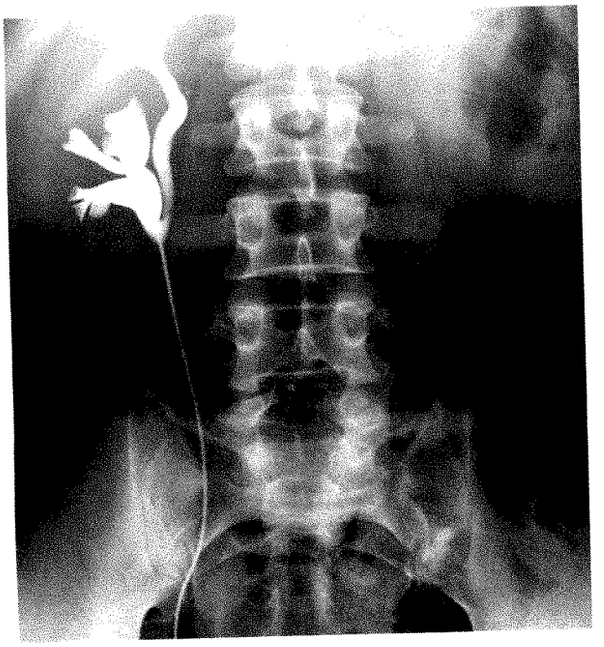
EASTMAN KODAK COMPANY
Radiography Markets Division
Rochester, New York

Quality commitment.

Just as you have a commitment to provide a quality diagnosis for your patients, Kodak has a commitment to provide quality x-ray products for all of your diagnostic needs.







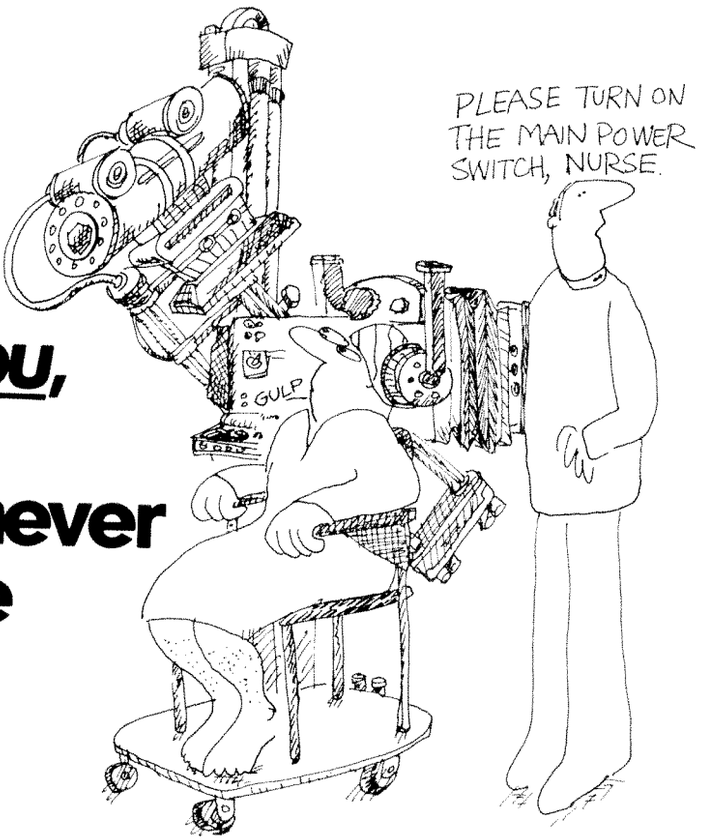
KODAK *RP* X-OMAT Medical X-ray Film offers maximum diagnostic detail as seen in the above left. Note the foreshortened colon secondary to previous surgery. In this exam, pathological changes involving the primary descending colon below the splenic flexure most likely represent a recurring tumor.

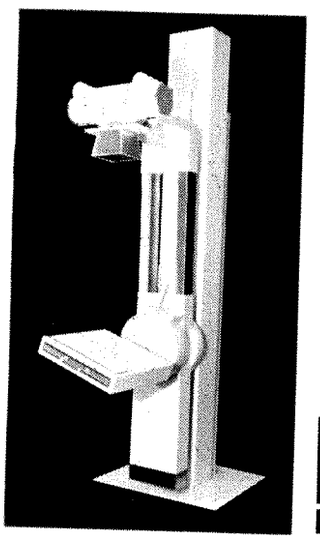
KODAK *RP/L* X-OMAT Medical X-ray Film visualizes a wide range of tissue differences. In the above, osteoblastic metastases from the prostate are easily distinguished. Normal cancellous bone, changes in the sacrum, erosion of the inferior pubic surfaces, and the surrounding soft tissues are all shown.

KODAK *RP* ROYAL X-OMAT Medical X-ray Film is for exams requiring high speed combined with sharp detail as viewed at left. The right kidney shows a bifid renal pelvis and calyces; no masses are present in the upper pole.

Kodak

It may not bother *you*, but the patient's never seen one before.





The subject of the day is radiographic headstands. Our message is simple: You now have an alternative. An alternative that is versatile, accurate, easy to operate, rock-solid. And most important, one that *looks* like the modern, carefully engineered, "painless" accessory that it is. May we send you complete information on the new Automatic Seriograph headstand? It could very well reduce your patient's anxiety, not to mention your own.

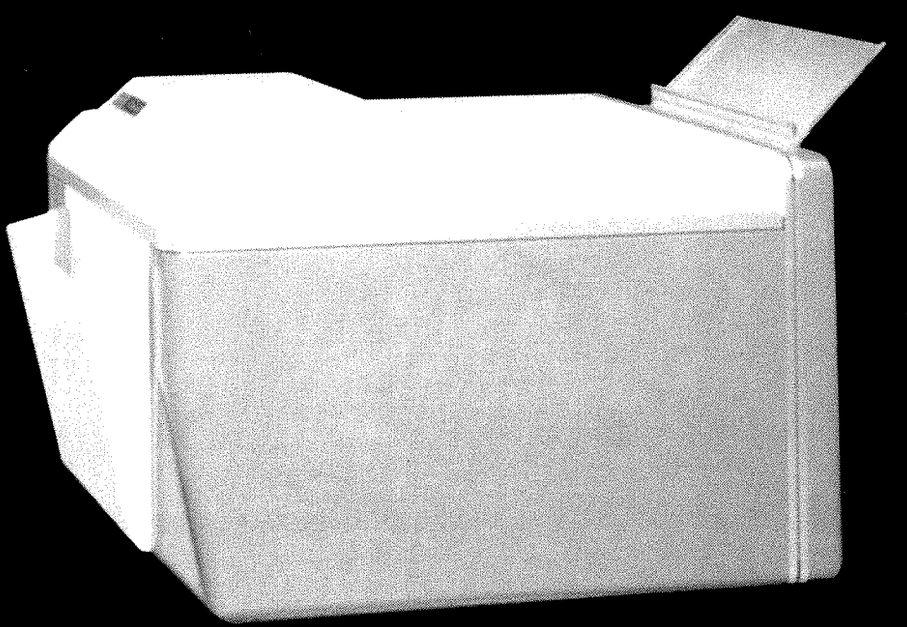
Litton

AUTOMATIC SERIOGRAPH

Des Plaines, Illinois 60018

New Pakorol-14X

SMALL SIZE ▪ LOW COST ▪ BIG CAPACITY ▪ HIGH QUALITY
AUTOMATED PROCESSING/DRYING



Regardless of where you want to process and dry medical X-Ray film— in the hospital, at the clinic, or right at the office, the new Pakorol-14X is for you.

LOOK AT THESE FEATURES!

- Low low cost = Only $4200 U.S. User Net
- Big Capacity — up to 120 — 14 x 17 films per hour. Handles sizes 5 x 7 to 14 x 36.
- Excellent quality results
- Dry to dry time — 2 min. 15 sec.
- Small size — Only 37 inches long x 22½ inches wide
- Portable — Plugs into any standard 115 volt, 20 amp service
- Use it on a table top, set it on a stand, use it on a convenient counter area.
- Plus — many more features such as:
  new rollerless crossovers
  new replenisher system
  new rack transport design

This new Pakorol-14X offers the precision processing and drying of X-rays that is so important to medical applications — and it does it fast, easily and with consistant top quality results.

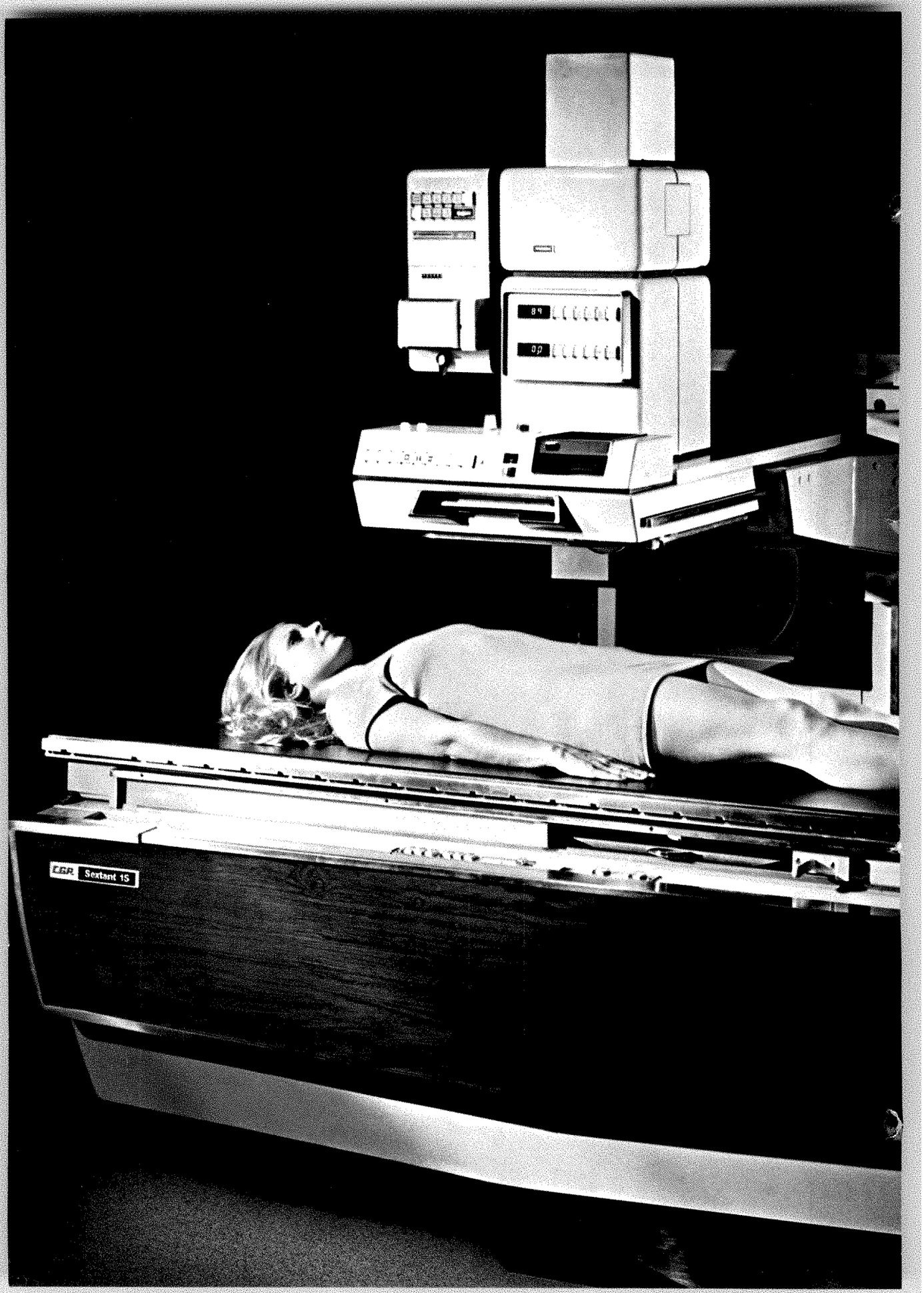
Best of all, the new low cost puts the Pakorol-14X right into your budget and leaves some left over for accessories like the special floor stand and others.

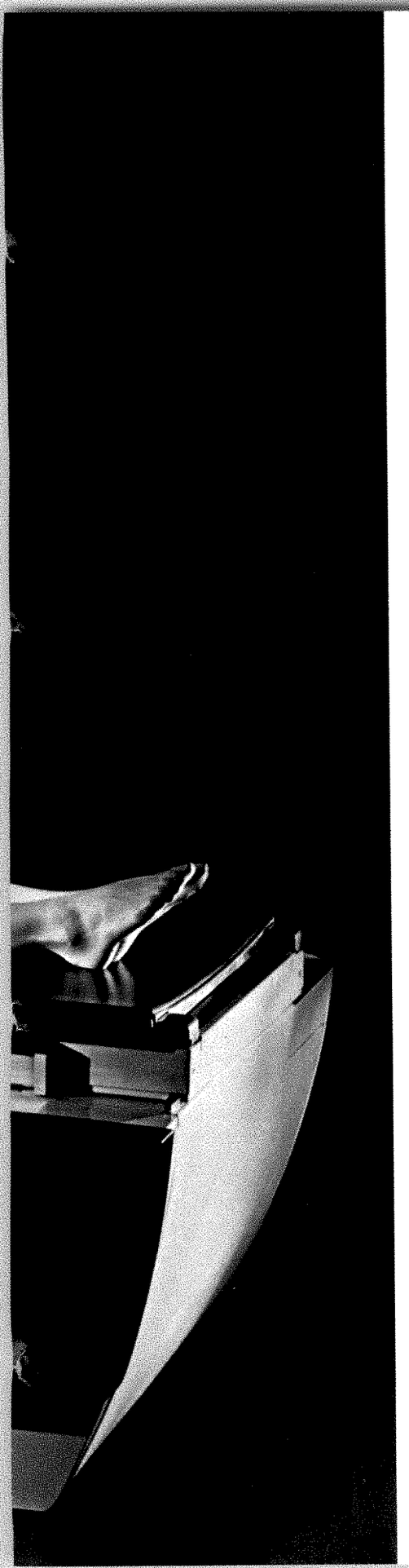
Ask your Pako Distributor about the new Pakorol-14X, or contact Mr. David Thoele at Pako Corporation for super fast action.

PAKO®

X-RAY PRODUCTS

PAKO CORPORATION
6300 Olson Memorial Hwy., Minneapolis, Minn. 55440


EGR Sextant 15



The Sextant 15 is the full-powered, fast mover in integrated diagnostic x-ray.

The toughest part of x-ray is the bull work you have to do with patient and equipment. The brutal, physical effort necessary to get results.

CGR's new Sextant 15 has changed this. It leads a new movement for fast, effort-free examinations. A complete, integrated 90°/15° radiographic-fluoroscopic diagnostic x-ray system.

Sextant 15 lets you move.

Its unique, self reliant tower assembly totally supports the spot film device and your choice of single or three port image systems. A single handle moves the spot film assembly longitudinally, transversely and for compression. Quickly. Easily. Using CGR's exclusive TriJet air power drive. A push button automatically parks or moves the spot film device to "field" position. You park without having to remove the image system.

Sextant 15 lets you speed your examination. The front panel is your command module. Everything push-button controlled. Automatic sequencing of 1 on 1, 2 on 1 longitudinal and transverse and 4 on 1. A "skip" push button for complex formating. A rapid exposure push button that eliminates the "park" position between exposures — lets you perform a 4-1 exposure sequence in less than 3 seconds. And a push button to retract or maintain the built-in oscillating grid.

The system has many additional features — all designed to improve, simplify and speed your examinations. Your CGR representative has all the information.

CGR MEDICAL CORPORATION
2519 Wilkens Avenue, Baltimore, Maryland 21203, (301) 233-2300

CGR CANADA LTÉE-LTD.
500 Boulevard de l'Aeroparc, Lachute, Quebec, Canada, (514) 562-8806

Show this processor ad to your fingers and your feet.

This part is for your fingers . . . With Sakura's QX-1200 X-ray film processor, you can change from 90-second to 3½ minute processing by just pushing a button. No other processor has this feature, which makes the 1200 a bit of good news for your fingers.

For you, the 1200 provides a big output from a small unit (only 5.5 square feet of floor space), is easy to operate and service, and gives you years of low-maintenance operation. It has direct developer and dryer temperature readings, and offers automatic feed for roll and cut film as an option.

This part is for your feet . . . Sakura's QX-Matic-S 3½ minute processor is ideal if you've developed aching feet from walking to a centralized processor.

The QX-Matic-S lets you decentralize. You can put a QX-Matic-S in the operating room, you can put one in the emergency room, you can even put one in the special procedures room. And since they only cost about $4000 each, you can do it without putting your budget into a bind.

The processor can be converted to two minute operation without extra cost. An optional automatic feed and take-up for roll and cut film eliminates hand feeding. There's also a self contained replenishing system for developer and fixer that operates automatically.

Easy to clean, easy to service, easy to operate and easy to get to. That's the QX-Matic-S.

Isn't that feet and shoulders above what you have now?

This part is for your head . . . If you'd like further information, send for our catalog.

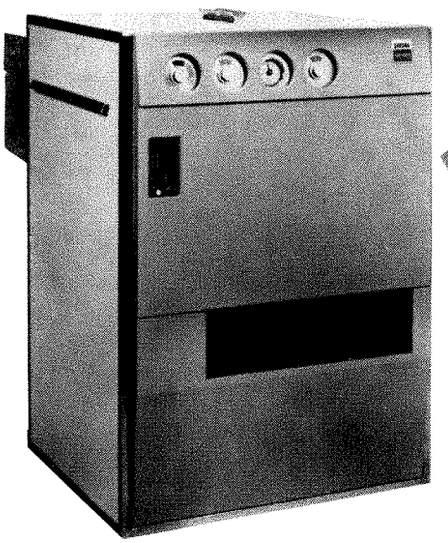
Keuffel & Esser X-Ray, Inc., 750 Huyler St., Teterboro, N.J. 07608.

KEUFFEL & ESSER X-RAY, INC.
X-Ray Film and Instrumentation

Exclusive Distributors
Western Hemisphere

SAKURA

FOR YOUR FINGERS





FOR YOUR FEET

information compendium

GENERAL ELECTRIC

Performance underscores GE's emphasis on innovation

Encompasses service, financing, systems planning too

General Electric's total concept of performance begins with a broad range of medical systems.

Then, to optimize equipment capability, GE provides in-depth systems planning, a variety of financing options and service programs known for keeping procedure schedules on schedule.

Now, insight into GE performance is provided in a new full color motion picture. It provides brief demonstrations of the systems shown on the following pages, and other systems too. Ask your GE representative for a desk top showing, scheduled to your convenience. Or, mail the coupon.

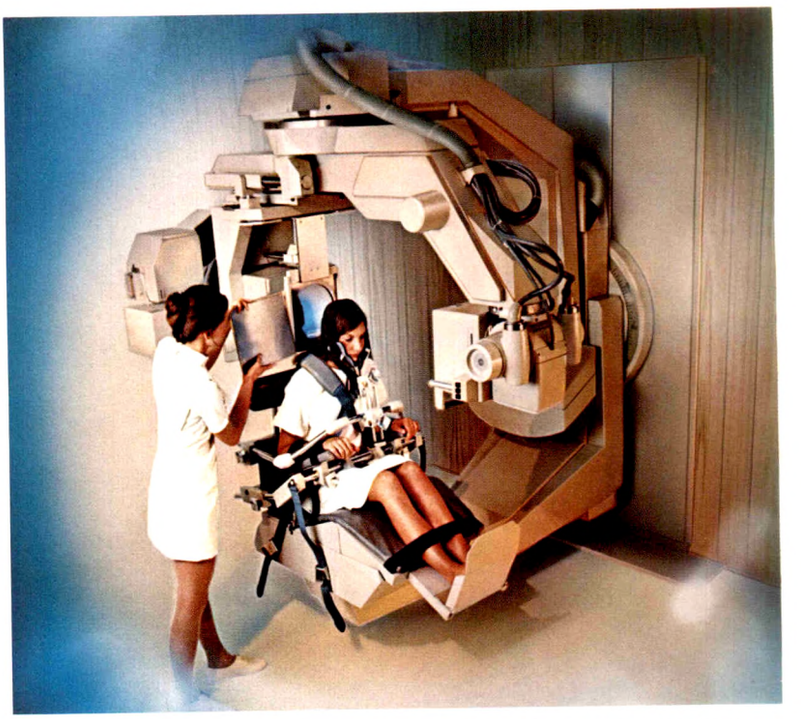
New Medical Systems Broaden Range of Diagnostic Capability

A dramatic demonstration of GE performance, over a broad range of diagnostic needs, is presented in four recently introduced systems...

New Neurological Diagnostic System

For comprehensive neurological procedures suites, GE's Neurotome™ system features continuous isocentric patient alignment on the desired region of interest. The system maintains this alignment for the complete series of views during pneumoencephalography, ventriculography and many other neuro examinations.

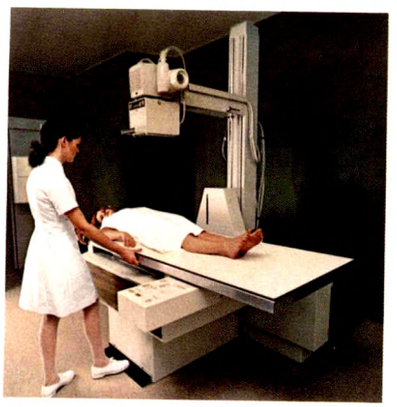
Neurotome significantly reduces patient handling and positioning, with the result that total procedural time is shortened, compared with less sophisticated systems. One reason is positioning flexibility. The patient can be rotated through a continuous ±450°; support arm for the tube, intensifier and cassette holder rotates through ±215°; and the isocentric chair features powered X-Y-Z motions.



This flexibility permits a series of linear tomograms at any angle of incidence, to effectively eliminate the common linear streaking on the long axis of the anatomy. Image intensification, coordinated with the 105 mm photospot camera, lets you dynamically view, then record, filling of the ventricles. Also, a cantilevered table permits supine examinations, such as neuro and arch angiography, as well as routine skull radiography.

New Radiographic/ Tomographic System

A high volume system that performs a variety of procedures in a short time. That's the RT Table.



This system permits the full range of routine radiography, plus true linear tomography and zonography; with instant push button procedural changeover.

RT Table integrates a motor driven tube stand and collimator plus motor driven cassette tray. Minimal object-to-film distance: 1.2 inches. All controls are convenient from table front. The tube unit angulates to 45° for special technics; and, with the tomo bar disconnected, permits routine radiography down length of table plus cross table technics and off table chests.



New Radiograph Illumination System

Fluoroline® Mobilview illuminator systemizes film loading and viewing.

Because all films are magazine-loaded in the processing area then rolled to the viewing station in the reading room, radiologists can spend more time interpreting and conferring, with no film handling.

In seconds, Mobilview powers two panels into viewing position; each panel displaying up to four 14 x 17 inch films, and 28 panels in all. Provides push button random access to each set of panels. A moving spotlight permits more definitive viewing of specific areas of films.



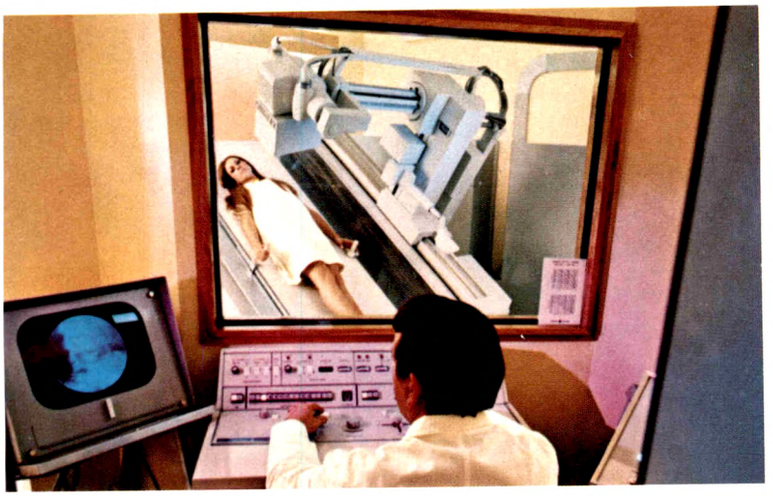
New Two-Probe Whole Body Scanner

Scans from head to toe, or anywhere in between, comprise the performance range of GE's Maxiscan™ two-probe whole body digital scanner.

Procedural set-up time is shortened because the operator's movements, between gantry and electronics console, are minimized. Maxiscan permits minification of a big 6 foot 8 inch patient to one fifth size; also one-half, one-third and one-fourth reductions plus 1:1 ratio scans.

Maxiscan's two probes scan an entire organ, such as the lung, top and bottom, without turning the patient. The top probe angulates through 270° and travels 12 inches vertically. With optional vertical plane scanning, upright patient scans can be accomplished, plus vertex views of the brain with the patient reclining normally.

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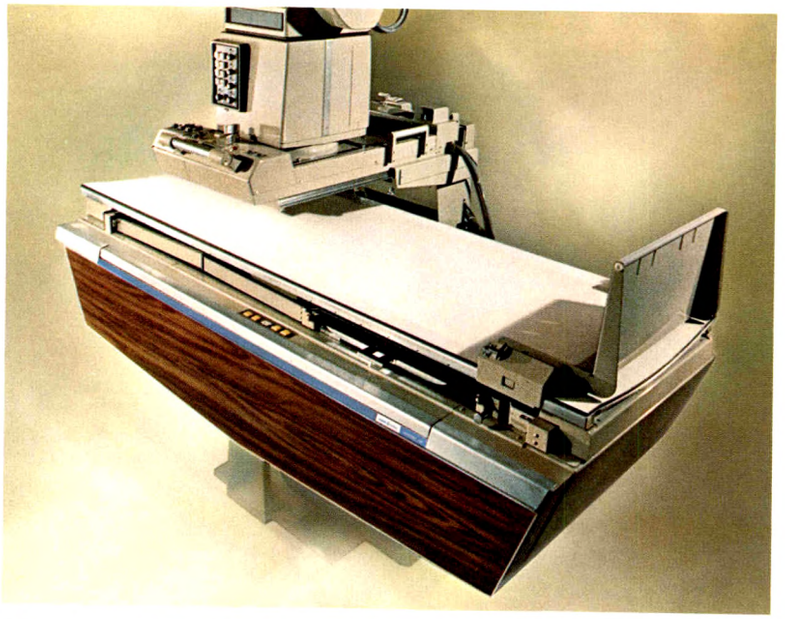
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ALFRED GELLHORN, M.D., D.Sc. (Hon)

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THE BACKGROUND AND PROMISE OF TUMOR VIROLOGY, IMMUNOLOGY, AND CHEMOTHERAPY AND A CHALLENGE TO RADIOTHERAPY*

JANEWAY MEMORIAL LECTURE

By ALFRED GELLHORN, M.D., D.Sc.(HON)†

I AM privileged to join you in honoring Dr. Henry H. Janeway 60 years after he took charge of cancer surgery and radiation therapy at the Memorial Hospital in New York. James Ewing in the first Memorial Lecture in 1933 spoke of Janeway's "scientific imagination, indomitable will and untiring industry—and a strong confidence in the ultimate capacity of radiation to control cancer."[18] That he was in part correct is a matter of the record achieved by you, the members of the American Radium Society, and your predecessors. That he was not wholly correct is attested by the bitter statistic of 350,000 deaths from cancer annually in the United States. Spurred by the incidence and death rates from neoplastic diseases and by the Congressional declaration "that cancer is the disease most feared by Americans today,"[31] the National Cancer Attack Act of 1971 has become the law of the land with a dramatic increase in Federal funding for cancer research.

The National Panel of Consultants on the Conquest of Cancer was persuasive and impressive when it stated in its report to the Senate Committee, "There have been major advances in the fundamental knowledge of cancer in the past decade, and these advances in knowledge have opened up far more promising areas for intensive investigation than have ever heretofore existed. These areas of special promise must be explored with vigor, if we are to exploit the great opportunities that lie before us."[48] Rhetoric or reason, that is the question.

Viruses, immunology and chemotherapy were among the identified aspects of particular expectation and in the hope of gaining some perspective on future developments in cancer research, I have made a personal analysis of these areas of promise which, for your better or your worse, will be shared with you. At best this may help to order your own thoughts on the subjects, at worst you will learn not to listen to the unlikely combination of a Dean-former cancer researcher again.

* Presented at the Fifty-fourth Annual Meeting of the American Radium Society, in Joint Session with the James Ewing Society and the Society of Head and Neck Surgeons, Boca Raton, Florida, May 14–19, 1972.

† Dean of the School of Medicine and Director of the Medical Center, University of Pennsylvania, Philadelphia, Pennsylvania.

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TUMOR VIROLOGY

In less than 100 years biomedical science has proceeded from the groping concept of a microorganism which was unlike anything previously known to the confident claim of the viral etiology of at least some human malignant tumors. What were, and are, the developments which led from obscurity to discoveries with mounting speed and what are the implications for cancer?

In 1884 Pasteur said that he was tempted to believe that rabies was caused by a microorganism which is infinitesimally small.[45] Ten years later a Russian, Iwanowski[33] and a Dutchman from Delft, Beijerinck,[8] independently discovered that a destructive disease of tobacco leaves could be transmitted by a bacteria-free filtrate of the sap of involved plants. The late Wendell Stanley, 37 years later in 1936, ground up one ton of tobacco leaves with this tobacco mosaic disease and, after many purifications, obtained crystallin virus.[53] Had that great and brilliant virologist and cancer researcher appropriately distributed the crystalline material, he could have eliminated the major cause of cancer deaths among men by destroying all tobacco plants throughout the world. But science must be served, so he provided some of his precious material to the British biochemists Bawden and Pirie,[7] who discovered that the virus consisted of a central core of nucleic acid surrounded by a bulky coat of protein. The relationship of the nucleoprotein virus and nucleoprotein genes was immediately perceived, but the startling implications of this general chemical similarity awaited the revolutionary developments in molecular biology initiated by the discovery of the structure of DNA by Watson and Crick.[56]

The story of tumor virology is fascinating not only because of its contemporary relevance, but also because it demonstrates the tremendous inertia of the conventional scientific wisdom which requires mountainous evidence and time to move it ponderously from one fixed position to another. As we review the literature,[23,25] we in medicine and science can readily identify with the human race characterized by Mark Twain in his comment, "Man is the only animal that blushes—or needs to." Our discomfiture now is due to the conviction of our predecessors that the cause of cancer was unknown and therefore, it was reasoned, a cancer caused by a known etiology was, by definition, a counterfeit. Let's skim the peaks of research performance which gradually changed the scientific posture.

In 1898 Sanarelli,[50] showed the viral etiology of lethal malignant myxomas in rabbits raised in the laboratory, demonstrated that the virus was endemic in the wild rabbit population in which it only produced a harmless fibroma due to immunological protection, and called attention to the transmission of the virus by mosquitoes. Armed with the magic vision of the retrospectroscope, it is apparent that the current surge in tumor immunology could well have begun 75 years ago. Further, Sanarelli's observations anticipated the demographic evidence of Denis Burkitt[11] which intimates that the African lymphoma is a viral disease passed by an insect vector.

The next malignant tumor to be shown to be due to a virus was leukemia in chickens.[15] With this animal model it was learned that the virus, or variants of it, could produce multiple types of neoplastic disease in fowl,[25] that the disease could be transmitted at the moment of fertilization of the ovum,[25] thus long pre-dating the oncogene theory popularized by Huebner,[32] and that chickens could be protected from the disease by appropriate vaccines.[25]

Then the magnificent Peyton Rous added a building block to the tumor virology edifice about which many more were to be placed. His discovery of the viral etiology of a chicken fibrosarcoma[49] provided him with an experimental model which he used imaginatively and productively for 50 years and countless other researchers followed his lead. The advances made using this virus-tumor system included the dem-

onstration of the virus by electron microscopy:[9] the observation that the virus could transform normal cells to malignancy *in vitro*, the determination that the Rous sarcoma virus has an RNA core unlike the others thus far studied which had a DNA core, that the virus does not respect the species barrier but produces tumors in rats, guinea pigs, deer and fish[59] and finally, in this enumeration, that it can exist in a state of dormancy in apparently normal cells, but be activated by a chemical carcinogen. This is only a very partial catalogue of the significant knowledge elicited with the Rous virus, but despite the growing literature on tumor virology, the facts were generally regarded as aberrant phenomena in the field of infectious diseases of birds and therefore unrelated to the real life problems of cancer in man.

The discovery by John Bittner that mouse mammary breast cancer was caused by a "factor" which was passed from mother to offspring in the milk,[10] the further finding that this factor could be seen in the electron micrograph and was an RNA virus and, in recent months, the report in the public press that a similar virus particle with the same biochemical characteristics had been found in human milk have shifted the previously prevailing winds of skepticism into a fresh breeze of confidence that a viral etiology of cancer in man will be proved quickly. Acute leukemia has long been a candidate for the viral enthusiasts and Ludwig Gross' demonstration that a virus was the cause of an acute leukemia in mice[26] has added circumstantial conviction to the human viral cancer concept.

But what of the evidence for viruses as a cause for human cancer? Is it only (with apologies to the other species) that we recognize that we are a part of the animal kingdom and therefore by analogy similar etiological mechanisms should be generally applicable? No, it is not as vague as this, although the methodology for proving the contention is necessarily limited to indirect probes.

Ever since the introduction of the electron microscope there has been a search for viruses in human tumor specimens. Reports have been published by Dmochowski of Baylor of particles compatible with virus in a variety of human tumors,[12,13] by Fink *et al.*[20] in plasma from leukemic patients, and by Moore *et al.*[42] in human milk showing ultramicroscopic objects which could be viruses. The obvious difficulties with these observations were that there was insufficient material to carry out alternative independent analysis to confirm the morphological evidence. Even if it is established that the viruses thus far seen are human-related, the possibility that they may merely be a passenger virus without direct etiological significance to the human tumors cannot be excluded.

The epidemiologic evidence for a viral etiology of human neoplastic disease is limited and far outweighed by the negative evidence. The most suggestive epidemiologic study was that of Burkitt who described the high frequency of a lymphoma of African children (none over 15 and most under 7 years) in a belt from the East to the West Coast of Africa, but only in low, hot, moist areas. Remember the rabbit myxomatosis and the mosquito vector of the virus? This sounded reminiscent and many studies have been carried out. Electron microscopy revealed a virus subsequently shown to be a known DNA herpes virus previously described by Epstein and Barr and antibodies to the virus are present in high titers in 87 per cent of affected persons as compared to 14 per cent in controls.[17,30,36] Now 2 other discoveries have been made with this strange Epstein-Barr virus. It is also associated with nasopharyngeal carcinoma[29] and it, or a close relative, appears to be the etiologic agent of infectious mononucleosis.[44] Whether we are dealing with an etiological agent or an incidental passenger virus in the human cancers is still moot.

Other immunologic evidence of viral oncogenesis in humans is limited. In the past year Wood and Morton[57] found an antigen common to human liposarcomas,

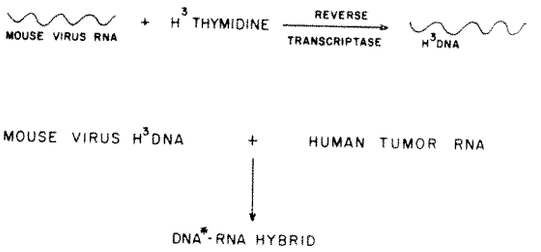


FIG. 1. Schematic flow diagram of the experiments of Spiegelman[4,38,57] to demonstrate the presence of a viral genome in human tumor chromosomes. Using the RNA mouse mammary tumor virus or the Rauscher mouse leukemia virus in the presence of tritiated thymidine and the appropriate enzyme, a DNA copy is made. The labelled mouse virus DNA is then incubated with RNA isolated from human tumor and if an RNA-DNA hybrid forms this is strong evidence that the human tumor chromosomes contained DNA indistinguishable from the mouse virus DNA.

osteosarcomas, and fibrosarcomas in a high proportion of patients with these tumors and their families in contrast to only 20 per cent in normal blood donors. Although this is compatible with a T-antigen due to a virus common to all the tumors, it could also be rationalized by other mechanisms as will be discussed later.

The evidence for a viral etiology of cancer derived from the concepts and techniques of molecular biology should be presented. A few years ago, Spiegelman demonstrated that when complementary RNA and DNA were incubated together, they would hybridize and this hybrid could be quantified. In a creative series of observations, Spiegelman and his colleagues have applied this technique to the study of the question of the presence of a virus in human neoplastic disease. More precisely stated, the issue is whether or not there is in the chromosomes of human tumor cells a viral genome which is directing the synthesis of RNA molecules. Capsulized, the experiments consist of synthesizing a tritium labelled DNA using the mouse mammary tumor virus (MMTV) and the Rauscher mouse leukemia virus RNAs as templates. The appropriate radioactive DNA is then incubated with RNA isolated from human leukemia cells, human breast cancer cells or a variety of sarcomas (Fig. 1). In each instance the Spiegelman group has reported that the hybridization is significantly greater between the mouse virus derived DNA and the human tumor RNA than between the isotopic DNA and control RNA.[4,27,38] These very recently published results of Spiegelman and his colleagues have not yet been confirmed and there are important questions of methodology and interpretation which will require further study. In fact, Dan Moore, a collaborator with Dr. Spiegelman in the human breast cancer studies, has recently expressed concern regarding the possibility of MMTV contamination of the human milk and other artifacts.[14,51] Nevertheless the provocative nature of the evidence and the boldness of the experimental concept must be acknowledged and applauded.

Now finally there is a clinical observation which is compatible with, but not conclusive of, a viral etiology of acute leukemia. Fialkow and colleagues[19] at the University of Washington have reported the case history of a 16 year old girl with acute lymphoblastic leukemia refractory to chemotherapy. She received 1,000 rads whole-body irradiation followed by a well matched bone marrow infusion from a brother. The graft was successful as evidenced by repopulation of the marrow only by donor cells with the XY sex chromosome markers. Sixty-two days after the marrow graft, the leukemia recurred and the leukemic cells carried the donor XY markers.[19] There may be many explanations for this dramatic occurrence, but a possibility is activation of a leukemogenic virus in susceptible donor cells or transfer of the virus from host to donor cells. The former possibility would be compatible with the experimental evidence of infection at the moment of conception as noted in the case of the avian leukemia or the mouse leukemias.

Viruses cause cancer in experimental animals with regularity when the conditions are appropriately manipulated, and viruses cause cancers in animals under

natural conditions as in the case of the fowl leukosis. The evidence that any human malignant neoplasm is caused by a virus is circumstantial or as yet only tentative. Is it so important to know? If the human tumor virus is transmitted in the genomes of the germ cells as in the case of the mouse leukemias and polyoma virus, then cancer cannot be prevented by a vaccine. If human tumor viruses are transmitted by insect vectors or in the milk as in the case of rabbit myxomatosis or the mouse mammary cancer, then *ad hoc* measures will be required in each instance. Thus prevention of all cancers through immunologic or chemotherapeutic control of a tumor virus seems unlikely, but specific knowledge would of course be of importance for diagnosis and possibly for antiviral therapy in special instances. Far more significant, however, in the field of tumor virology is the knowledge that can be gained using these extraordinary molecules to teach us how a cell is transformed from normal to malignant. The secret is contained in the genetic information of the oncogenic viruses and they have only 7 to 50 genes as compared with the 2,000,000 or more genes in human cells. What then is going on in this critical, fundamental area of investigation?[2,41]

The oncogenic DNA viruses include the *papova* group (*pa*pilloma, *po*lyoma, *va*cuolating SV40), adenoviruses which are frequent causes of upper respiratory infections in man but produce sarcomas when injected into newborn hamsters, herpes virus, and pox viruses. Most readily studied *in vitro* has been cell transformation by polyoma and SV40 with the following results:

a. Adsorption to the cell membrane and penetration to the cytoplasm. This step implies that the viral protein coat is not merely a protective envelope, but has configurations which lead to its discriminatory cell attachment and also enzymes which may be important in the process of penetration.

b. The protein coat is divested at the nuclear membrane.

c. A whole or a part of the viral DNA is inserted into the host cell genome, where and how not yet known.

d. An early viral gene product is a virus-specific T-antigen which appears in the nucleus, but is not in the virus itself. The function of the T-antigen is not yet known, but it does serve as a useful marker of viral transformation.

e. There is loss of environmental controls and most notably contact inhibition. In association with this phenomenon there appear new proteins on the cell surface among which there are tumor-specific transplantation antigens which are not present either in the normal cell or in the transforming virus. It is attractive to speculate that these cell surface proteins so modify the regulatory signals back to the nucleus that the orderly and controlled replication of cells is distorted with the resultant production of a neoplastic cell. Whether this is in fact the fundamental mechanism of uncontrolled growth has not, however, been established.

The oncogenic RNA viruses, also called leukoviruses or oncarnaviruses are, as earlier described, involved in the fowl leukemias and Rous sarcoma, the mouse mammary carcinoma, mouse leukemia and mouse sarcomas. A great puzzle was how an RNA virus could lead to the heritable transformation of cells which required some permanent change in the chromosomes. In 1964, Temin, an important contributor to virus research, proposed that there must be an enzymatic mechanism whereby the usual synthesis of RNA from a DNA template would be reversed such that DNA would be synthesized from an RNA pattern.[54] Less than 2 years ago David Baltimore,[5,6] and Temin and his colleagues,[55] independently found just such a reverse transcriptase and it was discovered to be one of the proteins of the viral coat. On the basis of this new evidence and other information gathered regarding the life cycle of the RNA viruses, a sequence of events similar to that of DNA virus transformation can very tenta-

tively be perceived. The RNA viruses attach to and then penetrate the normal cell membrane. The protein coat is shed and the RNA dependent DNA polymerase or reverse transcriptase catalyzes the synthesis of a DNA replica of the virus RNA. This is incorporated into the chromosomes and there may follow virus directed synthesis of cell surface proteins and a reassembly of the virus components with ultimate budding from the cell surface. This sequence differs strikingly from the DNA viruses in that cell transformation and virus replication can occur simultaneously, whereas the DNA virus cycle leads either to cell transformation or, alternatively, virus formation associated with cell death.

Is cancer a disturbance in the cell membrane with change or loss of signals to the nuclear machinery from the periphery? Is it due to the introduction of new genetic information, Huebner's oncogene, which when activated subverts the nuclear control mechanisms? Is it the result of derepression of genetic information which was active in embryonic life? These and other possibilities are now closer to direct study than ever before through the exquisite developments in tumor virus research.

TUMOR IMMUNOLOGY

Tumor immunology shares center stage along with oncogenic viruses and cancer chemotherapy as an area of research in which a major breakthrough is anticipated. Now that we have evaluated the likelihood that tumor virology will take the play away from all others, let us take a closer look at tumor immunology.

In the early part of this century when transplantable tumors first began to be widely used in cancer research, excited reports appeared of the regression of such tumors when transplanted from one strain of mice to another. The sweet taste of success and visions of speech-making in Stockholm turned to ashes when it was quickly shown that this was merely a manifestation of homograft rejection.

The pendulum quickly swung from the belief that there were host defenses against malignant disease to the concept of the completely autonomous cancer cell and its defenseless host. It has taken almost a half century for evidence to accumulate in diverse systems to recognize that a host-tumor interaction does occur and that there may be possibilities to give the host the advantage.

Tumors do form antigens which are not detectably present in normal tissues of the tumor bearing host and therefore may be considered specific. In the earlier discussion on viruses it was noted that the viral genome can direct the synthesis of the nuclear T-antigen and membrane antigens both of which are specific for the tumor virus regardless of the type of tumor that may be produced. You will recall that Wood and Morton[57] and Morton *et al.*[43] have reported antibodies to a common antigen in a number of patients with malignant melanoma and with osteogenic sarcoma. Another tumor-specific antigen unrelated to a possible virus is the identification of an antigen specific to hepatomas and another specific to the carcinomas of the gastrointestinal tract including pancreas which are not present in adult tissues, but which do exist in the embryo.

In 1963, the Russian oncologist, Abelev,[1] first demonstrated the presence of an alpha fetoglobulin in carcinogen-induced hepatomas of mice. Subsequently he and later Alpert[3] in this country showed that the phenomenon was not limited to mice, but that humans with hepatomas also had an antigen present in fetal liver. Although the reagents to test for this antigen are now commercially available, the diagnostic value is limited in this country because of the happy infrequency of primary liver cancer. The finding, however, of genetic information being expressed in a malignant tumor which is repressed in the adult nor-

mal cells, but is operational during fetal life provides fascinating possibilities for exploration of the fundamental mechanism of neoplastic growth. Another example of this phenomenon is the widely heralded observation of Gold and Freedman[24] of an antigen present in human gastrointestinal cancers which also exists in human embryos, the carcinoembryonic antigen. Early reports indicated a high per cent positivity in patients with cancer of the colon, but more refined clinical studies have shown only 45–55 per cent positive in localized tumors, in contrast to the 90 per cent positive assays in cases with metastatic disease. In those patients with apparently localized disease, who do have demonstrable circulating carcinoembryonic antigen, surgical excision of the tumor is followed by disappearance of the antigen. This may offer a sensitive indicator for recurrent disease.

Although Gold originally reported that the CEA was specific for entodermal tumors, there are reports of positive tests in a variety of other human malignancies and also in severe alcoholic cirrhosis and alcoholic pancreatitis.[58] Whether the identical or closely related antigens are being detected in these diverse conditions cannot be stated for certain as yet. Despite these reservations, it is likely that there will soon be available to all a valuable immunological test for certain cancers.

Experimental tumor immunology suggests that unique antigens appear in neoplastic cells, and yet very carefully manipulated experiments are required to demonstrate host immunological defenses. Why should this be? The answers are not all in, but the possibilities include: (1) the tumor antigen may be located only in the nucleus and therefore not available to stimulate the generation of circulating antibodies or specifically sensitized lymphocytes; (2) the antigen may not be strongly antigenic; (3) cell surface antigens may stimulate the synthesis of humoral antibodies and of sensitized lymphocytes, but the antibodies merely cover the antigenic sites without harming the cell, while preventing the killer lymphocytes from recognizing the tumor cell. This is the "blocking antibody" hypothesis of the Hellströms[28] and has much to support it.

Despite these limitations, immunotherapy holds many attractions because of its great potentiality for specificity, and therefore increasing effort is being devoted to its study and application.

Specific immunotherapy may be conceived as the stimulation of immune reactions directed against tumor associated antigens. For reasons already discussed this is not yet a practical approach in man since no tumor specific antigen has been isolated in order to test its efficacy in autoimmunization. When and if this becomes possible the question of antigenic potency can be evaluated and, if this is low, chemical modifications may well be made which would increase antigenicity. In the meantime, the efforts in human neoplastic disease have been directed toward nonspecific immunotherapy, that is, the general stimulation of the host immune reactions.

Thus far, tumor associated antigenicity or lymphocyte-mediated cytotoxic reactions have been demonstrated for Burkitt's tumor, leukemias, melanomas and neuroblastomas. The long time remission and even apparent cure of the African lymphoma following chemotherapy has been speculatively related to the ability of the host immune defenses to destroy the small number of tumor cells remaining after the chemotherapeutic regimen. This and experimental evidence led Mathé[40] to mount a pilot experiment in 1964 with control and experimental groups of children and adults with acute leukemia. All patients received as effective chemotherapy as possible to achieve hematologic remission and in addition were given intrathecal chemotherapy and appropriate radiotherapy to forestall meningeal exacerbation. Thirty such patients in remission were

then randomized into control and experimental groups, the latter receiving BCG injections of irradiated leukemic cells from a pool. The results showed a significant prolongation of the remission interval in those receiving nonspecific immunostimulation.

Final assessment of this and other clinical trials will have to be deferred, but the considerable amount of experimental animal evidence certainly provides a basis for encouragement and further refinements are likely to improve results. Also a word of caution: there is experimental evidence that the immune reaction may stimulate tumor growth in certain circumstances so, as in the case of most therapeutic measures, we are dealing with a two-edged sword.

CHEMOTHERAPY

The discovery of drugs which objectively produce remissions of a variety of malignant tumors in man has had a tremendous impact in clinical cancer which far transcends their demonstrable effect on the statistics of cure or survival. In the broad sense, the chemical attack on cancer has dramatized the fact that only about one-third of all patients with neoplastic disease are cured by surgery and radiotherapy, leaving the vast problem of disseminated malignancy as the major target of research. Despite the apparently disappointing statistical validation of the oft-repeated hopes for cancer chemotherapy over the past 30 years, the eminent Dutch cancer researcher, Professor Emmelot recently wrote, "Cancer chemotherapy seems at last to begin to come of age developing from an art into a science."[16] Admittedly Dr. Emmelot does not allow his enthusiasm to be unrestrained, but his view is generally accepted by those most closely associated with clinical and laboratory tumor chemotherapy. Lets try to catch the sense of the field in a brief glance.

Table 1 presents many of the clinically used anti-tumor drugs divided into classes. Although this is not a complete listing, it will amply serve to illustrate the current concepts.

There are three general mechanisms of cytotoxic action of these drugs:

1. The alkylating agents and perhaps Procarbazine react with DNA thereby preventing normal replication at the time of cell division. These compounds can produce their toxic effect regardless of the cell cycle phase and if the damage is not repaired by the time of division cell death will occur.

2. The antimetabolites and antibiotics interfere with DNA synthesis by a variety of mechanisms and are, therefore, dependent upon the S phase of the cell cycle for their cytotoxic action.

3. The third mechanism is the large category of "Don't know for sure." It is possible that the Vinca alkaloids interfere with spindle formation during the mitotic cycle as evidenced by metaphase arrest, but this is not certain. The hormones have multiple possible actions to account for their quite specific antitumor effects including suppression of the anterior pituitary, enhancement of cellular maturation, and inhibition of cellular metabolism, but precise understanding is lacking.

L-asparaginase is in a class by itself for it acts indirectly on those tumor cells which lack asparagine synthetase by destroying exogenous asparagine on which the tumor cell is dependent.

Some of you who may have reached the alarming stage of your speaker when events of 30 years ago seem like yesterday will recall the 1940 dramatic clinical reports of Huggins and Erbst on androgen control therapy of prostatic cancer with estrogen, and even more exciting, the release of information on the use of the previously "classified drug" HN_2 in the effective treatment of the lymphomas in 1946, of aminopterin in acute leukemia in 1948, and then the beginning flood of nitrogen mustard derivatives. By the mid 1960s almost all of the classes of the clinically useful agents had been introduced and

TABLE I

CLASSIFICATION OF CHEMOTHERAPEUTIC AGENTS USEFUL IN NEOPLASTIC DISEASE

Class	Type	Non-proprietary Names
Alkylating agents	Nitrogen mustards	Mechlorethamine (HN_2, mustargen) Cyclophosphamide (cytoxan, endoxan) Melphalan (L-sarcolysin, alkeran) Chlorambucil (leukeran)
	Ethylenimines	Triethylenethiophosphoramide (Thio-TEPA, TSPA)
	Alkyl sulfonates	Busulfan (myleran)
Antimetabolites	Folic acid analogs	Methotrexate (amethopterin, MTX)
	Pyrimidine analogs	5-fluorouracil (5fu) Cytarabine (cytosine arabinoside, ara-c, cytosar)
	Purine analogs	6-mercaptopurine (6MP, purinethol) 6-thioguanine (TG)
Natural products	Vinca alkaloids	Vinblastine (VLB, velban) Vincristine (VCR, oncovin)
	Antibiotics	Mitomycin C Dactinomycin (actinomycin D, cosmegen) Daunorubicin (Daunomycin)
	Enzyme	L-asparaginase
Miscellaneous		Procarbazine (n-methyl hydrazine, MIH, natulan) Hydroxyurea (hydrea)
Hormones		Estrogens Androgens Progestins Adrenocorticoids

their effectiveness had been assessed in various disseminated human malignancies. So many hopes were raised by the demonstration of objective remissions in lymphomas, leukemias, certain childhood tumors, and a few solid tumors in adults, only to be dashed by the brevity of the response and the toxicities of the drugs which limited retreatment. But persistent studies on the mechanism of action of the drugs and other pharmacological aspects together with research on cell kinetics and the life cycle of normal and tumor cells began to change the dreary picture. The men and women who have worked so steadfastly at the bench and at the bedside despite the many disappointments merit recognition and honor.

With the use of experimental models of mouse leukemia, Skipper and his colleagues showed that an antileukemic drug such as Methotrexate could cure the disease when given in tolerated doses so spaced that repair of hematopoietic and intestinal epithelial damage could occur before proliferation of leukemic cells had reached pretreatment levels. This principle was applied to the treatment of childhood acute lymphoblastic leukemia by clinical investigators in collaborative programs and significant extensions of remission intervals measured in periods greater

Table II

I. CANCERS IN WHICH SOME PATIENTS ARE CURRENTLY ACHIEVING NORMAL LIFE EXPECTANCY
Acute lymphoblastic leukemia in children
Combination chemotherapy for Hodgkin's disease and other lymphomas
Choriocarcinoma
Testicular carcinoma
Embryonal rhabdomyosarcoma
Ewing's sarcoma
Wilms' tumor
Burkitt's lymphoma
II. CANCERS THAT ARE SUBSTANTIALLY RESPONSIVE TO CHEMOTHERAPEUTIC AGENTS BUT WHERE LONG TIME SURVIVAL HAS NOT BEEN DEMONSTRATED
Hormonal therapy for breast cancer
Single and combination non-hormonal chemotherapy in breast cancer
Surgical adjuvant therapy for breast cancer
Ovarian cancer
Acute myelocytic leukemia in adults
Chronic myelocytic and chronic lymphocytic leukemia
Multiple myeloma
Neuroblastoma
III. CANCERS THAT SHOW LIMITED RESPONSIVENESS TO CHEMOTHERAPEUTIC AGENTS BUT LONG TERM SURVIVAL HAS NOT BEEN ACHIEVED
Head and neck cancer
Lung cancer
Gastrointestinal cancer
Malignant melanoma
Central nervous system cancer
Endocrine gland cancer

than 2 years were achieved. Then an early series of observations by Goldin and his colleagues on the use of combinations of antitumor drugs with different mechanisms of action was introduced into the clinical trials so that the cell cycle concept of Skipper and the multimechanism cytotoxicity of Goldin were joined. An indication of the current status of cancer chemotherapy is perhaps best given by an outline of the program for the National Conference of Cancer Chemotherapy to be held in June, 1972 (Table II).

Table II reveals much and also speaks eloquently of the unknown. Tumor cells with a rapid proliferation rate such as acute leukemia and the lymphomas as well as some of the childhood tumors are susceptible, but malignant melanoma, osteogenic sarcoma and acute myelocytic leukemia, also aggressively multiplying cells, are not. The cancer chemotherapists, encouraged by their successes, however, look to greater understanding of cell pharmaco-receptors and better methods for measuring cell cycle rates in individual patients as fruitful areas to improve their attack on disseminated tumors. These combined with the collaboration of radiotherapy, surgery, and immunotherapy give hope to the 100 per cent kill approach to cancer therapy.

Is there any other possibility to consider in cancer therapy? Yes, I think so, and with your permission I will briefly present my bias—not in so much detail as to bore, alarm, or anger you, but hopefully to prophesy the future. There is evidence that malignant tumor cells of man, other animals, and plants retain the full genetic information of normal cells.[21,22] The inappropriate hormone secretion syndrome in which a wide variety of nonendocrine tumors may produce polypeptide hormones indistinguishable from normal; the change in phenotype as in the common phenomenon of squamous metaplasia in adenocarcinomas; the experimental demonstration that a single anaplastic tumor cell has the multipotentiality for the production of many normal cell lines;[37] the demonstration by transplantation of a tumor nucleus into an enucleate ovum that normal embryogenesis can occur;[35] the reversibility of neoplastic transformation by an oncogenic virus when the virus is lost;[39] and the expression of an embryonic antigen in gastrointestinal, breast, and liver cancers —all these varied evidences in human and experimental cancers point not only to the retention of normal genetic information, but also indicate that the neoplastic transformation is not irreversible. However, can this be controlled? This past year has been marked by what may be a beginning. Three

groups of investigators, A. Johnson *et al.*,[34] Sheppard,[52] and Prasad and Hsie[46,47] have found that morphological differentiation and return of contact inhibition can be induced in fibrosarcoma and neuroblastoma cells in tissue culture with the addition of cyclic AMP. If this heralds the beginning of controlled pharmacological action on the expression and repression of gene information, it is conceivable that one day the therapeutic approach to cancer will be revolutionized toward differentiation of the malignant cell rather than toward its destruction.

CONCLUSION

This brings to an end our review of 3 principal areas of research. There are many other important fields such as chemical carcinogenesis, epidemiology, tumor-host relationship, cell biology and radiobiology with significant implications for prevention and cure, but I don't believe that an examination of the current state of knowledge in these subjects would modify our conclusions.

In my opinion the fundamental question in cancer research is not the cause, because we already know multiple causes; it is not the cure, because we already know multiple ways in which it may be cured; it is instead, "What is it?" When we are able to answer this question, we will quickly be able to determine whether cancer is one or many diseases, we will know whether prevention can be achieved by one fundamental mechanism or whether we will have to protect against physical, chemical and biological etiologies (a task which boggles the imagination), and finally we will be able to assess the likely future of radiotherapy, surgery, chemotherapy, and immunotherapy. As one of the principal curative modalities, I believe that the discipline of radiation therapy is secure for a long time. Do not, however, relax. Your assignment in the universe of biomedical research is as great as of any other specialty, but, additionally, you must identify even more closely with society's needs of this day.

Time does not permit an in-depth consideration of the crisis in the availability of medical care in America now, but of this you are aware. In the field of radiotherapy, I perceive 2 critical issues which the public expects you to resolve: (1) the dearth of trained clinical oncologists with the special skills of radiotherapy; and (2) the availability of effective radiotherapy for all those who need it regardless of socioeconomic status or geographical location. Will you accept the challenge of providing the remedies to these deficiencies? Contemporary medical education with its increased elective time, with its acceptance of multiple curricular tracks provides you the mechanism whereby you can encourage the interest of young men and women while still they are medical students in your discipline. With imagination and resolve, the recruitment of students to the challenging field of oncology and radiotherapy with its potentialities for basic research, for clinical medicine, and for meeting great human needs should show results quickly. This kindling of the interest early in the medical career of the physicians of tomorrow necessarily must involve you in more teaching which not only serves an important end, but multiplies the value of your personal clinical experience.

The equitable availability of radiotherapy will require the development of a system or systems which are oblivious to socioeconomic considerations and will solve the problems imposed by geography. Already medical economics is forcing the development of radiation treatment centers and this trend will undoubtedly be accelerated by impending health insurance legislation. As leaders in clinical medicine you can facilitate the evolution of such systems of medical care delivery in this country. You best know the cost and complexity of the equipment needed for cancer therapy, you know the varieties of

back-up service that are required, you know the importance of a multidisciplinary approach and, therefore, yours is the responsibility to play an important architectural role in American medicine of tomorrow.

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INCIDENCE AND CAUSES OF FAILURES TO CONTROL BY IRRADIATION THE PRIMARY LESIONS IN SQUAMOUS CELL CARCINOMAS OF THE ANTERIOR TWO-THIRDS OF THE TONGUE AND FLOOR OF MOUTH*

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IN almost all publications on results of treatment of cancer, only survival rates are given with no analysis of the sites of failure; *i.e.*, failure to control the primary lesion or regional lymphatic disease or distant metastases. To determine causes of failures in order to improve methods of treatment, the first step is to know the sites of failures.

In a previous publication[5] on squamous cell carcinoma of the oral cavity, the analysis of the sites of failure, *i.e.*, primary, neck, etc. was done, but no attempt was made to find the possible causes of failure. In this paper, the analysis will be directed to correlate results of treatment with the extent of the primary disease and the irradiation techniques.

CLINICAL MATERIAL

The clinical material consists of the squamous cell carcinomas of the oral tongue (that part of the tongue which is in front of the circumvallate papillae) and the floor of the mouth, treated from January 1948 through December 1968. The squamous cell carcinomas of the base of the tongue (that portion of the tongue back of the circumvallate papillae) have a drastically different behavior and, therefore, are considered as separate clinical entities. The diagnosis of the site of origin is obvious except in massive lesions involving the whole tongue. In those cases, the differential diagnosis can usually be made on the clinical features of the disease.

The analysis was made in April 1971, all patients having a minimum of 2 years follow-up, 90 per cent of them having 5 years or more follow-up. A minimum of 2 years follow-up for a small number of the patients is adequate for evaluation of control of the primary lesion, as 90 per cent of the recurrences appear by 3 years. If active disease appears in the vicinity of the original lesion at any time during the follow-up, be it 10 years after the initial treatment, it is counted as a failure.

The staging is as follows:

T_1—Tumors less than 2 cm.* in diameter
T_2—Tumors 2 to 4 cm.* in diameter, no invasion of surrounding structures
T_3—Tumors more than 4 cm.* in diameter, and/or invasion of surrounding structures
T_4—Massive tumor or bone involvement.

The combined policy of the Department of Radiotherapy and the Section of Head and Neck Surgery at the M. D. Anderson Hospital has been to use irradiation as the initial treatment for the majority of patients with oral tongue lesions, reserving

* Prior to July 1965, 3 and 5 cm. were used instead of 2 and 4 cm. The lesions have been re-staged accordingly.

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surgical procedures for failures. Lesions in alcoholics and heavy smokers are preferentially treated surgically because of the individual's poor tolerance to irradiation. Lesions, less than 1 cm. and well demarcated, of the lateral border of the tongue, small lesions of the dorsum or tip of the tongue, and superficial lesions associated with leukoplakia are treated by simple excision, since in these clinical situations it will entail little loss of tongue. Moderately sized lesions in very old patients who tolerate partial glossectomy better than irradiation and for whom impaired speech is not important, are at times excised.

The reasons for the choice of treatment of the primary lesion for the floor of the mouth are subtle. By and large, irradiation is preferred as floor of the mouth lesions are very readily controlled by irradiation. Very small lesions are simply excised for a variety of anatomic reasons, and in the alcoholic (a high percentage of patients with floor of the mouth lesions are inveterate alcoholics). Sometimes a very narrow arch, a forward slant of the arch or tori preclude a good radium implantation, or periosteal involvement increases the risk of necrosis. In these situations, a surgical procedure may be preferred.

IRRADIATION TECHNIQUES

Most lesions of the oral tongue have always been treated by interstitial radium implants alone or combined with external irradiation. External irradiation alone has been used in patients with lesions of the oral tongue from Stages T_1 through T_3, when there was contraindication to general anesthesia.

The same techniques were used for the floor of the mouth lesion. Some superficial lesions of the floor of the mouth, contiguous to the alveolus in edentulous patients in whom the floor of the mouth is flat, have been treated by intraoral cone therapy using 150 kv. In recent years, the 6 to 9 mev. electron beam has been used, the tumor dose being 5,500 to 6,000 rads in 4 to 5 weeks.

Some patients with lesions of the floor of the mouth were selectively treated since 1963 by an electron beam submental field alone. Some other patients did not have interstitial gamma-ray therapy, at least as part of the treatment, because of contraindication to general anesthesia.

The technique of interstitial radium therapy and the combination with external irradiation were outlined in a monograph published in 1962.[6] Interstitial radium therapy was the treatment of choice for T_1 lesions; the combination of external and interstitial irradiation was routinely used in the more advanced lesions in order to buffer the swing of dose unavoidable from large implants. The interstitial radium implants were done first, followed by external irradiation. The arrangement of radiation sources did not follow Paterson and Parker distribution rules and the method of calculation, although derived from the Paterson and Parker system, was not identical to it.

In December 1961, a retrospective analysis was made of the volume distribution of interstitial radium implants obtained by computer dosimetry.[7] A correlation was found between "cold spots" and recurrences, and between necroses and areas receiving high doses and high dose rates.

From 1961 on, a generous minimal tumor dose was selected from the computer isodoses knowing that the doses could be as much as 20 per cent higher than the doses given in earlier years. An analysis in January 1963 showed an increased incidence of complications; the doses were reduced by 10 per cent with a less generous minimum tumor dose. During the following 2 years (1963 and 1964), there was a decrease in complications, but the local recurrence rate increased in patients with the oral tongue lesions, but not in those with the floor of the mouth lesions. From January 1965 on, different total doses and dose-time factors have been used for lesions of the oral tongue and those of the floor of the mouth.[3] If an early lesion can be encompassed by a small or moderately sized implant, 2,000 rads tumor dose is given with external irradia-

TABLE I

ANTERIOR-TWO THIRDS OF TONGUE
FAILURE TO CONTROL THE PRIMARY LESION IN PATIENTS TREATED BY DEFINITIVE IRRADIATION
(Unlimited Follow-up*)
January 1948–December 1968
(Analysis April 1971)

Stage	No. of Failures on No. of Patients	Patients Salvaged by Surgery†	Percentage of Ultimate Failures
T_1	5.7% (3/52)	1/3	5.5%
T_2	17.0% (17/100)	5/17	12.0%
T_3	41.0% (27/66)	6/27	32.0%
T_4	67.0% (20/30)	2/20	60.0%
Total	27.0% (67/248)		21.3% (53/248)

* Squamous cell carcinoma developing at any time after the follow-up in the vicinity of the initial lesions are counted as recurrences.
† NED (no evidence of disease) at 2 years after treatment of failure.
5 year survival rates: {absolute 45% / determinate 52%}.

tion as a preneedling dose in 5 to 6 treatments; in the moderately sized lesions, 3,000 rads in 3 weeks to 5,000 rads in 5 weeks tumor dose is given with external irradiation prior to needling, the higher dose being given to large lesions and to those so located that a good geometric implant is unlikely to be achieved. Every attempt is made to see that the dosage rate is no more than 40 rads per hour, 25 to 30 rads being preferred if 5,000 rads have been given with external irradiation.

RESULTS

ORAL TONGUE

Table I shows the failure rates by T staging, the number of failures salvaged by a surgical procedure and the ultimate failure rates. There is a rapid increase in the incidence of failures from T_1 to T_3 lesions.

In Table II, the analysis of failures by modality of irradiation shows that external irradiation alone is not an effective method of treatment for lesions of the oral tongue. Interstitial radium therapy alone or the combination of external irradiation and interstitial therapy seemingly produce approximately the same results from T_1 through T_3, but, by and large, the worse lesions had the combined treatment.

In Table III, some specific causes of failure are shown in the T_1, T_2, and T_3 lesions. There is no need to explain failure of treatment for the massive T_4 lesions. Poor geometry with "cold spots" could be

TABLE II

ANTERIOR TWO-THIRDS OF TONGUE
FAILURE TO CONTROL THE PRIMARY LESION BY MODALITIES OF IRRADIATION
January 1948–December 1968

Stage	No. of Failures on No. of Patients	External Irradiation Only	Interstitial Irradiation Only	Combined External and Interstitial Irradiation
T_1	5.7% (3/52)		3/48	0/4
T_2	17.0% (17/100)	4/9	9/55	4/36
T_3	41.0% (27/66)	10/17	3/10	14/39
T_4	67.0% (20/30)	10/15	4/6	6/9

TABLE III

ANTERIOR TWO-THIRDS OF TONGUE
SPECIFIC CAUSES OF FAILURES
January 1948–December 1968

Stage	No. of Failures	Combined External and Interstitial Irradiation	External Irradiation Only
T_1	3	2 cold spots 1 ? implantation	
T_2	17	8 no obvious cause 2 ? implantation 2 poor geometry 1 geographic miss	3 no obvious cause 1 patient with leukemia, palliation with low dose
T_3	27	11 no obvious cause 5 palliative implants 1 ? implantation	9 no obvious cause 1 patient with intraarterial 5-FU (actually T_4)

identified in 4 patients, and in another 4 patients there was a suggestion of implantation of viable tumor cells pushed by the needles (in 1 of these 4 patients, the recurrent disease was close to the hyoid bone). In the T_3 lesions, 5 patients had basically palliative implants. The patients treated with external irradiation only, either were poor medical risks or were treated palliatively.

The analysis of the relative incidence of failure by location, *i.e.* undersurface, lateral border, posterolateral border, could not be done because not all patients (primarily those treated in the earlier years) had an accurate description of the location of the lesion. However, patients whose lesions were on the posterolateral border of the tongue involving the faucial pillar probably had a somewhat higher failure rate. For several years it has been the practice in the posterolateral border lesions to add an extra plane going through the floor of the mouth and the anterior faucial pillar to

TABLE IV

FLOOR OF MOUTH
FAILURE TO CONTROL THE PRIMARY LESION IN PATIENTS TREATED BY DEFINITIVE IRRADIATION
(Unlimited Follow-up*)
January 1948–December 1968
(Analysis April 1971)

Stage	No. of Failures on No. of Patients	Patients Salvaged by Surgery†	Percentage of Ultimate Failures
T_1	2.0% (1/49)	1/1	0%
T_2	11.5% (9/77)	4/9	6.5%
T_3	23.0% (14/60)	11/14	5%
T_4	79.0% (19/24)	0/19	79%
Total	20.5% (43/210)		13% (27/210)

* Squamous cell carcinoma developing at any time after the follow-up in the vicinity of the initial lesions are counted as recurrences.
† NED at 2 years after treatment of failure.
5 year survival rates: {absolute 56.0% / determinate 67.5%}.

TABLE V

FLOOR OF MOUTH
FAILURE TO CONTROL THE PRIMARY LESION AND MODALITIES OF IRRADIATION
January 1948–December 1968

Stage	No. of Failures on No. of Patients	External Irradiation Only	Interstitial Irradiation Only	Combined External and Interstitial Irradiation
T_1	2.0% (1/49)	0/10	1/31	0/8
T_2	11.5% (9/77)	5/23	3/34	1/20
T_3	23.0% (14/60)	9/25	3/17	2/18
T_4	79.0% (19/24)	13/16	2/4	4/4

adequately treat involvement of the sulcus and the foot of the pillar.

FLOOR OF MOUTH

Table IV shows the failure rates by T staging, the number of failures salvaged by a surgical procedure, and the ultimate failure rates. The increase in the incidence of failures is not as steep from the T_1 to T_3 lesions as for those of the oral tongue. There is a high salvage rate by surgery and the ultimate failure rates are very low, even in the T_3 lesions.

Table V shows the failures by modalities of irradiation. A significant proportion of lesions were selectively treated by external irradiation only, usually submental electron beam alone or combined with parallel opposing portals with 22 mev. photon beam. Some of the lesions had external irradiation only because general anesthesia could not be given because of the poor physical condition of the patient. The results in the T_2 and T_3 lesions treated by interstitial radium implant or the combination of interstitial radium implant and external irradiation are slightly better than those with external irradiation alone.

Table VI shows some specific causes of failures for the T_1 through T_3 lesions. There are a few "cold spots" and geographic misses. In 1 instance, there was a recurrence in the submental space, probably because needles pushed viable tumor cells which produced an implant.

COMPLICATIONS

Soft tissue ulcers develop in a significant percentage of patients, primarily in those patients with floor of the mouth lesions. With simple care, the ulcers usually heal in a few months.

When the soft tissue ulcer is on or reaches the gum (primarily in floor of the mouth lesions), there is the complication of bone exposure. The management of bone exposures must be very conservative; it consists of good dental hygiene, removal of sequestra as they loosen, and extractions being done only when absolutely necessary.[1] From 1965 through 1968, with this program, the incidence of surgical procedures for bone necroses has been less than 10 per cent.

DISCUSSION

Among the few reports in the literature on the control rate of primary lesions, it seems that outstanding results have been obtained with interstitial implants.[9] Fayos and Lampe[2] reported that with using intraoral cone therapy, an 82.5 per cent control rate was achieved in 51 lesions less than 3 cm. in diameter, and 58 per cent in 24 lesions 3 to 5 cm. in diameter. Only 4 lesions in their series involved one-half of the tongue and there were no T_4 lesions. The control rates of the primary lesions cannot be compared with those reported by Saxena[10] because lesions of the base of the

TABLE VI

FLOOR OF MOUTH
SPECIFIC CAUSES OF FAILURES
January 1948–December 1968

Stage	No. of Failures	Combined External and Interstitial Irradiation	External Irradiation Only
T_1	1	1 no obvious cause	
T_2	9	1 no obvious cause 1 cold spot 1 ? implantation 1 Au^{198} (poor medical condition)	3 no obvious cause 2 inadequate dose (poor medical condition)
T_3	14	3 no obvious cause 1 SCC of vocal cord 4 yr. earlier; no external irradiation, implant unsatisfactory 1 cold spot	5 no obvious cause 3 geographic miss 1 underdosed

tongue and oral tongue are not separated in Saxena's report.

Our control rates of squamous cell carcinomas of the floor of the mouth are better, except for T_1 lesions, than those of the oral tongue. Our surgical salvage of the failures is also better. Since 1965, our failure rate for all lesions from T_1 through T_3, of the oral tongue and floor of mouth, is 10 per cent. This high control rate with few complications is due to computer dosimetry, low dosage rates, and adjustment for treatment times with conservative management of the teeth before and after treatment.[1] Interstitial gamma-ray therapy must be used, at least as part of the treatment for squamous cell carcinomas of the oral tongue and, if feasible, for most of those of the floor of the mouth.

Except for very early lesions, some external irradiation is given before the interstitial implantation to prevent implantation of viable tumor cells into the surrounding tissues by the needles passing through active cancer. A tumor dose of 2,000 rads in 5 or 6 treatments (equivalent to 3,000 rads in 3 weeks) destroys a very high percentage of the tumor cells, making seeding less likely.

The patients who received the combination of external and interstitial gamma-ray therapy were divided in 2 groups, those receiving less than or more than 4,000 rads with external irradiation and an appropriate dosage from interstitial implants. The control rate is the same for both groups. We now prefer giving 5,000 rads to the primary lesion (supplemented by an interstitial gamma-ray implant), to both the submaxillary triangles and subdigastric area lymphatics, with 5,000 rads given dose to the lower neck to those patients with a high risk of disease recurrence in the radically dissected neck and of appearance of contralateral metastases.[4,8]

SUMMARY

Interstitial gamma-ray therapy still is an important modality of irradiation for oral tongue and floor of the mouth lesions.

Computer dosimetry and careful dental hygiene result in a high control rate with few complications.

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Vol. 117, No. 3

RADIOTHERAPY OF ADVANCED CARCINOMA OF THE OROPHARYNGEAL REGION UNDER HYPERBARIC OXYGENATION*

AN INTERIM REPORT

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ALTHOUGH the role of oxygen in enhancing the radiation effect in many biologic systems has been well confirmed, a significant improvement in clinical results of radiotherapy of human cancer with application of oxygen is still to be established.

Attempts for restoring tissue oxygen tension in human tumors during radiotherapy include: (1) breathing pure oxygen under increased atmospheric pressure in a compression chamber;[5] (2) breathing oxygen and carbon dioxide (95 per cent and 5 per cent, respectively) under atmospheric pressure through a nose mask;[6,8] and (3) intra-arterial injection of hydrogen peroxide in the tumor region.[13]

A program for the clinical study of the effect of oxygen in the radiotherapy of human cancers was started at the Columbia-Presbyterian Medical Center in 1960.[14] The method of hyperbaric oxygenation was chosen because by breathing oxygen under high pressure (3–4 atmospheres, absolute), the partial pressure of oxygen in the arterial blood and the solubility of oxygen in physiologic solution may increase 20–30 fold.[11] Initially a compression chamber made of steel was used and operated at 4 atmospheric pressure. Eighteen patients with advanced cancers in various parts of the body were accepted for hyperbaric oxygen therapy as a pilot study with massive dose in 2 or 3 treatment fractions. Subsequently 11 more patients with locally advanced cancer of the upper food and air passages were accepted for hyperbaric oxygen treatment by randomization with control groups.[1]

In 1963 we acquired a new transparent pressure chamber made of lucite and manufactured by Vickers & Co. of London, England. The new chamber operated at a lower pressure of 3 atmospheres (absolute). This greatly reduced the frequency of convulsion due to oxygen toxicity and eliminated the need for general anesthesia. With elimination of general anesthesia, many more treatments can be given than with the previous 2 or 3 massive dose treatment techniques. However, with the increase of the number of fractions, reassessment of the time-dose relationship and biologic response is necessary.[3]

MATERIAL AND METHOD

A. *Clinical population.* For a meaningful comparison of the treatment results from 2 different methods, 2 identical testing populations are required. For instance, a pair of tumors ideal for such testing would consist of tumors in the same anatomic sites, of the same histologic type and grade, and at the same stage of development, *i.e.*, a more or less homogeneous population. To achieve this end, we selected only patients with previously untreated, biopsy proved, squamous cell carcinoma, arising in a few adjacent anatomic sites, such as the tonsillar fossa, soft palate, anterior faucial pillar, retromolar trigon, base of tongue and adjacent buccal mucosa. Essentially, these

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TABLE I

THE TNM STAGING SYSTEM FOR CARCINOMA OF THE OROPHARYNX

(Modified by MacComb and Fletcher[12])

Stage	Definition
T_1	Tumor less than 2 cm. in diameter
T_2	Tumor 2 to 4 cm. in diameter, with minimal extension to adjacent structures
T_3	Tumor more than 4 cm. in diameter with limited extension to adjacent structures
T_4	Massive primary tumor
N_0	No clinical evidence of lymph node metastasis
N_1	Clinically evident single lymph node metastasis less than 3 cm. in diameter
N_2	Single lymph node metastasis over 3 cm. in diameter or multiple ipsilateral lymph node metastasis
N_3	Large lymph node metastasis with fixation, or bilateral metastasis
DM	Distant metastasis

are carcinomas of the oropharynx as defined by MacComb and Fletcher.[12] In advanced stages, T_3 and T_4, this group of lesions usually involves several adjacent structures and may become a large confluent mass which is often indistinguishable as to its site of origin. The TNM staging system, as modified by MacComb and Fletcher,[12] is adopted (Table 1). Only T_3 and T_4 lesions are accepted in this study. Occasionally T_2 lesions are treated as another pilot study and are not included in this analysis.

B. *Experimental schemes.* Three treatment groups are assigned and patients are accepted to the treatment group by randomization.

1. OHP (Oxygen under High Pressure) Study Group. Patients in this group receive radiotherapy under hyperbaric oxygen at 3 atmospheres. The dose schedule is 600 rads per treatment for 6 treatments, totaling 3,600 rads, at a 2 treatment per week schedule for 3 weeks. The hyperbaric procedure has been described in detail previously.[4] The NSD (Nominal Standard Dose of Dr. F. Ellis)[7] for this group is 1,770 rets.

2. Control Group I. Patients in this group receive radiotherapy in atmospheric air. The dose schedule is 600 rads per treatment for 7 treatments, totaling 4,200 rads, at a 2 treatment per week schedule for $3\frac{1}{3}$ weeks. The NSD for this group is 1,875 rets.

3. Control Group II. Patients in this group receive radiotherapy in atmospheric air with conventional fractionation, *i.e.*, 200 rads per treatment for 30 treatments, totaling 6,000 rads, at a 5 treatment per week schedule for 6 weeks. For the past 3 years we have increased the dose from 200 to 220 rads per treatment for 30 treatments, totaling 6,600 rads, in 6 weeks, in order to produce comparable degrees of skin and mucosal reactions as those observed in OHP and Control I groups. The NSD in this group varies from 1,770–1,945 rets.

The addition of a conventional fractionation, as Control Group II in this study, serves 2 purposes: (a) to assess whether an observed greater tumoricidal effect, if it exists, in the oxygen group is due to oxygen or simply due to the unconventional greatly reduced fractionation scheme; and (b) to compare the results between the oxygen study group and the group treated with the best available conventional technique in air.

TABLE II

THE AGE AND SEX DISTRIBUTION IN THE STUDY SERIES

Age (yr.)	Male (no.)	Female (no.)
20–29	1	0
30–39	1	1
40–49	4	1
50–59	13	4
60–69	11	6
70–79	6	1
80+	1	1
Total	37	14

Male to Female Ratio = 2.5 to 1

TABLE III

CARCINOMA OF OROPHARYNGEAL REGION
ANATOMIC SITE AND STAGE DISTRIBUTION

(51 Cases)

Group	OHP (600 rads×6)		Air Control Group I (600 rads×7)		Air Control Group II (200–220 rads×30)	
No. of Cases						
Site	T_3	T_4	T_3	T_4	T_3	T_4
Tonsillar fossa and soft palate	8 (N_1, N_0, N_3, N_0, N_3, N_3, N_0, N_1)	1 (N_1)	3 (N_0, N_3, N_1)	0	6 (N_0, N_3, N_0, N_3, N_0, N_3)	0
Anterior faucial pillar, retromolar trigone, alveoli and adjacent buccal mucosa	4 (N_0, N_2, N_0, N_1)	1 (N_1)	2 (N_2, N_0)	0	0	1 (N_0)
Base and latero-posterior tongue	8 (N_3, N_0, N_1, N_1, N_1, N_0, N_1, N_1)	4 (N_1, N_2, N_3, N_1)	5 (N_2, N_0, N_0, N_2, N_0)	2 (N_1, N_3)	5 (N_2, N_0, N_3, N_0, N_0)	1 (N_1)
Total	20	6	10	2	11	2
	26		12		13	

The present series comprises 51 patients who were admitted to the program from January 1964 through March 1971. By randomization with sealed envelope technique, 26 were designated to the OHP study group, 12 to the Control Group I, and 13 to the Control Group II. The age and sex distribution of this series (Table II) shows that the ratio of male to female is about 2.5 to 1. There are more females in the control groups than in the oxygen group. Otherwise, the distribution of patients between the study and control groups is quite comparable. The tumor site and stage distribution (Table III) between the study and control groups are also quite comparable.

RESULTS

The treatment results are evaluated according to the rates of local tumor control, survival and complications.

1. *Clearance rate of primary tumors and cervical lymph node metastasis.* This means a complete local tumor regression for more than 6 months after the completion of radiotherapy (Table IV). A 65 per cent clinical clearance rate for primary tumor was noted in the OHP group *versus* 42 per cent in the Control Group I and 55 per cent in the Control Group II. A 23 per cent higher clearance rate for the primary tumor in the OHP group than in the Control Group I is noteworthy. There was only a 42 per cent clinical clearance rate for the cervical lymph node metastasis in the OHP group, and 29 and 25 per cent for the Control Group I and Control Group II, respectively. This low clearance rate for the cervical lymph node metastasis is not surprising, since our policy for the treatment of metastatic cervical lymph nodes is radical neck dissection; only a sublethal holding dose is delivered to the cervical

TABLE IV

CARCINOMA OF OROPHARYNGEAL REGION
CLINICAL CLEARANCE OF LESIONS
(>6 months)

	OHP (600 rads×6)		Control Group I (600 rads×7)		Control Group II (200–220 rads×30)	
Primary tumor (T_3, T_4)	65%	(18/26)	42%	(5/12)	55%	(7/13)
Cervical lymph node metastasis RND*	42%	(8/19) 10/26	29%	(3/7) 3/12	25%	(2/8) 4/13

* Radical neck dissection.

lymph nodes. However, in a few cases in which the cervical lymph nodes were situated within the primary treatment field and received adequate tumoricidal dose, there was evidence of clinical and histologic clearance of the metastatic lymph nodes, as demonstrated by subsequent radical neck dissection.

2. *Survival rate.* The survival rates were evaluated according to the actuarial (Life Table) method (Fig. 1). The 3 curves depict a slightly higher 5 year survival rate in the OHP group (38 per cent) *versus* Control Group I (25 per cent) and Control Group II (22 per cent). There are 6 patients in the oxygen group who have survived free of disease for more than 5 years. The 5 year survival rate for patients with T_3 or T_4 lesion is 38 per cent for the oxygen group which is not worse than in other reported series treated by conventional radiotherapy.

3. *Complication rate.* As we equate the tumor dose in order to produce a similar degree of skin and mucosal reaction in all 3 groups, there is no significant difference in the instance of severe mucosal reaction or delayed wound healing due to overdose to the mucosa or skin. The other important complications, such as, convulsion, radionecrosis of the mandible and distant metastasis are tabulated (Table v). In our experience, the incidence of convulsion due to oxygen toxicity is less than 1 per cent of the number of oxygen exposures. A 10 per cent incidence of radionecrosis of the mandible in the oxygen group is slightly higher than in the control groups, but all 3 patients have had radical neck dissection prior to the development of symptoms and signs of osteonecrosis. It is postulated that the radical neck dissection may have contributed to local trauma and further diminution of blood supply to the man-

TABLE V

CARCINOMA OF OROPHARYNGEAL REGION
COMPLICATION RATE FOLLOWING TREATMENT

	OHO (600 rads×6)	Control Group I (600 rads×7)	Control Group II (200–220 rads×30)
Convulsion	1	0	0
Radionecrosis of mandible	3/26	1/12	1/13
Distant metastasis	2/26	1/12	3/13

dible. The incidence of pulmonary metastasis in the oxygen group is not higher than in the air control groups.

REPORT OF A CASE

This 59 year old white male patient had an 8–9 month history of sore throat, and more recently blood-streaked sputum and a mass in the left side of the neck. An ulcerative tumor was seen in the soft palate with complete destruction of the uvula and with extension to the left tonsillar fossa, estimated to be about 5 cm. in the longest diameter (Fig. 2). There was a huge mass on the left side of the neck, about 11 cm. in the longest diameter, firm and fixed. There was another smaller mass of 3 cm. in diameter on the right side of the neck, partially fixed (Fig. 4). The biopsy from the primary tumor was reported as epidermoid carcinoma. The chest roentgenographic examination was negative. This case was staged as $T_3N_3M_0$.

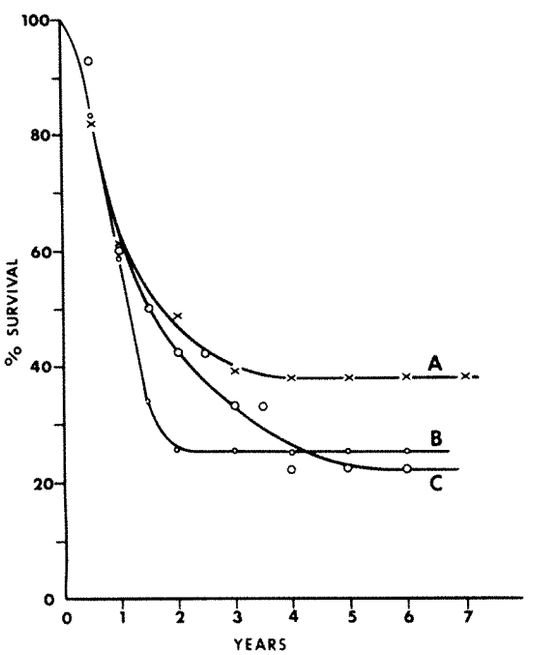


FIG. 1. Carcinoma of the oropharyngeal region—postradiotherapy survival rates.

Curve A. Hyperbaric Oxygen Study Group—600 rads per fraction ×6 fractions at twice per week schedule, NSD (nominal standard dose) = 1,700 rets.

Curve B. Air Control Group I—600 rads per fraction ×7 fractions at twice per week schedule, NSD = 1,875 rets.

Curve C. Air Control Group II—200–220 rads per fraction ×30 fractions, NSD = 1,770–1,945 rets.

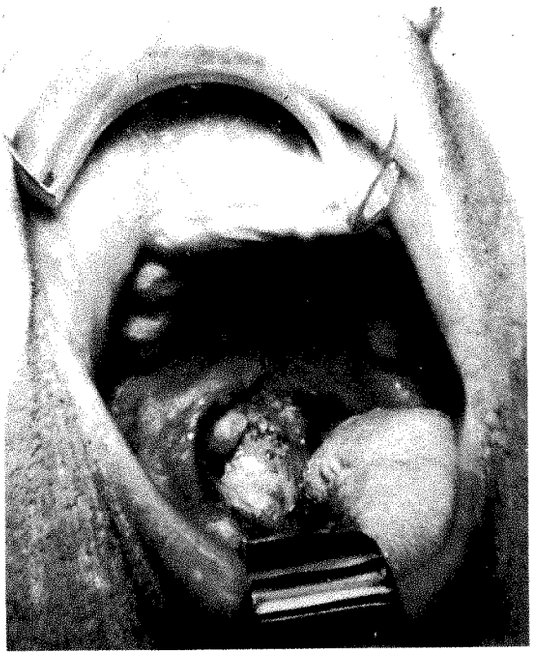


FIG. 2. An ulcerative tumor in the soft palate with complete destruction of the uvula and with extension to the left tonsillar fossa.

Radiotherapy was administered through lateral opposing 12×15 cm. portals in March 1967. An additional treatment was given to the left cervical mass, as it was declared inoperable 1 week after conclusion of the regular course of treatment. Each treatment consisted of 600 rads tumor dose given while the patient was breathing 100 per cent oxygen at 3 atmospheres (absolute). The tumor dose to the primary palatotonsillar lesion was 3,600 rads in 17 days at twice per week schedule. Following radiotherapy the primary lesion regressed, the membranous mucositis cleared in about 4 weeks and the ulcerative tumor disappeared (Fig. 3). The left cervical mass regressed slowly, but did not disappear, while the enlarged, right cervical lymph node completely regressed (Fig. 5). The patient subsequently developed a left medial clavicular lymph node enlargement and bilateral pulmonary metastases 8 months following the initial treatment and succumbed to the disease, while the primary lesion was still under control.

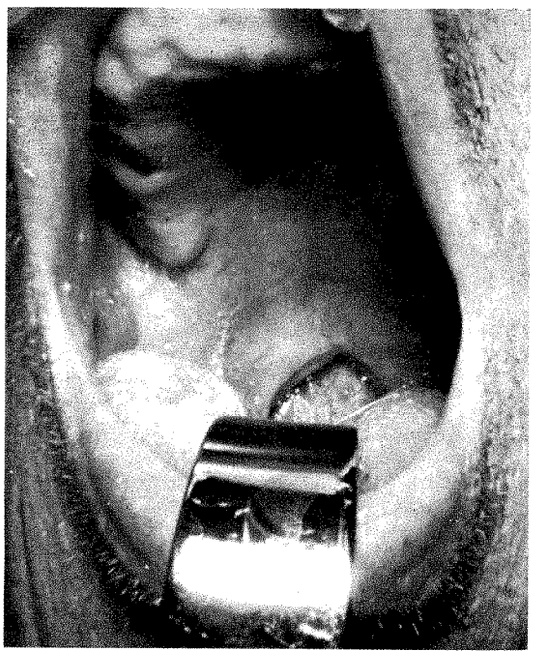


Fig. 3. Complete regression and healing of the ulcerative tumor in the soft palate and tonsillar fossa, about 4 weeks following hyperbaric oxygen radiotherapy.

DISCUSSION

The tumor dose for the Control Groups I and II was purposely designed to be higher than for the OHP Group by a factor of 10 to 15 per cent. This was due to our concern regarding that: (1) if the oxygen effect truly operates in the human tumor system, as it does in the experimental animal tumors, then we would have underdosed the patients who are randomized into the control groups and receive the same dose as given to the OHP group; and (2) if one should desire to equate the normal skin and mucosal reactions of the 3 groups to the same end points, it would be necessary to raise the tumor dose in the Control Groups I and II. When one interprets the results in our series, one must take these higher doses, given to the control groups, into consideration. Until very recently, Henk and associates[10] reported in a randomized trial for the head and neck cancer that there are higher survival rates and significantly higher local tumor control rates in the OHP group than in the air control group, at a follow-up period of 2–3 years. However, the number in their oropharyngeal cancer subgroup was small, about 15 in each OHP and control group. Evans and Sanfilippo,[8] on the other hand, recently reported that there was no significant difference in the local recurrence rate in a randomized series of advanced oral cavity cancer irradiated with or without atmospheric oxygen breathing through a nasal catheter. At present, most study series in various centers are still too small in patient number to draw a valid conclusion. In our present series, the observed difference in survival rate between the OHP and the air control groups is about 13 per cent which has no statistical significance at this sample size according to Boag's series of curves.[2] From these curves, it is found that for a 15 per cent difference between such 2 groups, it would require about 70 cases in each group in order to be significant ($P=0.05$). Therefore, if the trend of a 15 per cent difference can be

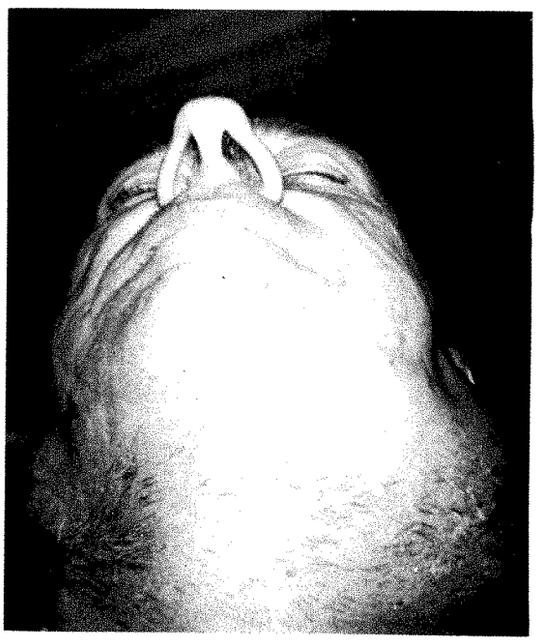


Fig. 4. A huge mass on the left side of the neck, about 11 cm. in longest diameter, firm and fixed. Another smaller node of 3 cm. in diameter on the right side of the neck.

maintained for the next 3–5 years, we may expect to have a significant study from this long going effort. In general, we feel that the clinical evidence is more encouraging than before, as regards the use of oxygen as an adjuvant to radiotherapy. We should remember that oxygen effect is just one of the factors which affect the response of tumors to x-irradiation. Therefore, we should not expect a spectacular change in cure rate by only restoring the normal oxygen tension to tumor cells. However, any small gain should contribute to the over-all goal of clinical management of cancer patients.

The complication rates and incidence of distant metastasis in our series were not higher than in the control groups.

The data from our Control Groups I and II are insufficient to make any statement as to whether the slight improvement of local tumor clearance rate in the Control Group II is due to the factor of reoxygenation operating through the conventional fractionation scheme.

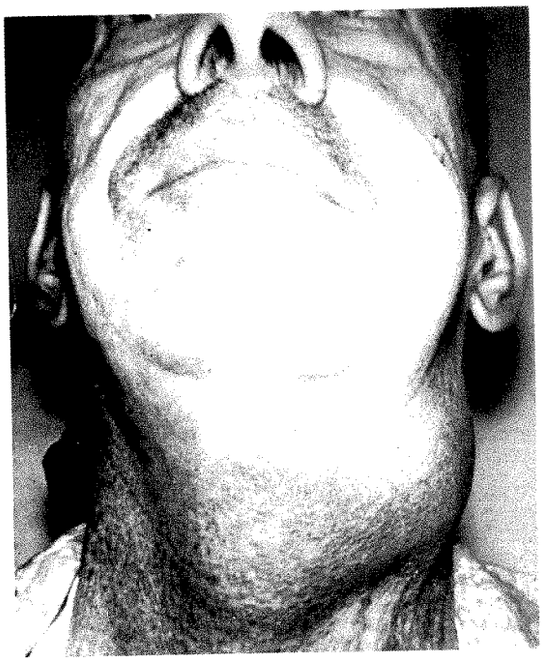


FIG. 5. Only partial regression of the huge metastatic left cervical mass and complete disappearance of the right smaller cervical node, 2 months following the conclusion of hyperbaric oxygen radiotherapy.

SUMMARY

This is an interim report of a clinical trial of radiotherapy of advanced oropharyngeal cancer under hyperbaric oxygenation.

Fifty-one cases are available for evaluation, 26 in the oxygen group, 12 in the Control Group I, and 13 in the Control Group II.

The results are analyzed as to: (1) clearance rates of the primary tumor, in which a 23 per cent higher clearance rate for the primary tumor in the oxygen group than in the air Control Group I is noted; (2) survival rates, in which a 13–15 per cent increase of the 5 year survival is revealed in the oxygen group, compared to the air Control Group I; and (3) complication rates and incidence of distant metastases which are not higher in the oxygen group than in the control groups.

Although the difference of local tumor clearance and the survival rates between the oxygen and the control groups are not statistically significant due to the small sample size, the evidence of improvement in both local tumor clearance and in survival rates from our series and from that of Henk *et al.*[10] favors the use of oxygen as an adjuvant in radiotherapy for advanced oropharyngeal cancer.

A cooperative study among many institutions for a meaningful and accelerated data collection is urged.

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CARCINOMA OF THE TONSIL AND NASOPHARYNX*

A 20 YEAR END RESULTS REPORT

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THIS series covers the period 1949–1969 and includes all cases of carcinoma of tonsillar and nasopharyngeal origin registered in the Province of Alberta during this time. There were 52 tonsillar lesions and 85 nasopharyngeal lesions. Of these, 11 tonsillar and 13 nasopharyngeal cancers were of nonepidermoid type and will not be further analyzed in detail. None were lost to follow-up.

In both sites, lesions classed as "anaplastic" or "transitional" carcinomas have been included as squamous cell carcinomas (S.C.C.). The distinction between S.C.C.s and lymphoepitheliomas has been maintained, although the view that the latter are nonkeratinizing S.C.C.s with lymphocytic infiltration,[7,14] is held by the authors. Only cases with positive histology, from the primary site at least, have been included.

The survival data are calculated from the date of the first treatment, and the gross survival figures have been adjusted only by correction for the life expectancy of each subgroup, analyzed according to the life expectancy tables of the general population as a whole. The effect of using this type of adjustment is to make the overall survival experience somewhat worse than using a so-called "determinate rate." In this paper, therefore, all cases not alive, or alive with disease at the various temporal end-points considered, are held to be "nonsurvivors." It is felt that this method of "age adjustment" is a more accurate and valid measure of the effect of therapy than the "determinate" or any other method which excludes from analysis cases that were lost to follow-up, died postoperatively or from other complications of the specific treatment given for the disease, or died from intercurrent disease in the periods being studied.

Staging throughout has been according to the U.I.C.C. T.N.M. Classification. Since this was applied retrospectively, certain errors were expected, and no doubt some have been made. In carcinomas of the nasopharynx, for example, "T" staging is not always exact. This had little impact, when it was decided to classify this disease simply as "T_2N_1 or better" and "worse than T_2N_1." In the case of tonsillar lesions, the retrospective information available gave sufficient data to be confident of almost 100 per cent accuracy in staging.

GENERAL CONSIDERATIONS

AGE INCIDENCE

The average age in both sites was consistent with other reports.

Lymphoepitheliomas occurred at a slightly younger average age in both sites (51 yr. for tonsil and 48 yr. for nasopharynx) than the other S.C.C.s (55 yr. for tonsil and 56.6 yr. for nasopharynx).

SEX INCIDENCE

Males outnumbered females 33:8 in tonsillar cancers. Males outnumbered females 52:20 in nasopharyngeal lesions.

ETHNIC CONSIDERATIONS

Seven cases with a diagnosis of nasopharyngeal cancer were known to be of Chinese or Eskimo extraction. While this is high in relation to their estimated pro-

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Table I

INCIDENCE OF CELL TYPE IN THE PRESENT AND COMPARABLE SERIES

Tonsil	Squamous Cell Carcinoma	Lympho-epithelioma
Present Series	83%	17%
Fayos and Lampe[5]	94%	5%
Scanlon *et al.*[11]	83%	17%
Nasopharynx		
Present Series	62.5%	37.5%
Chen and Fletcher[2]	55 %	45 %

portion of the population, (*i.e.*, 10 per cent of these cancers occurred in less than 1 per cent of the population), the numbers are too small to be anything but suggestive of a higher incidence of this disease in ethnic groups known to be susceptible to it.

TUMOR TYPE

The relative incidence of the 2 types under discussion is shown in Table 1. This was not significantly different from other series reported.

CARCINOMA OF THE TONSIL

MATERIAL AND METHOD

The 41 cases admitted to the series comprised only those in which there was little doubt that the primary tumor arose either in the fossa or the pillars. In this case material, only 3 cases without tumor in the fossa itself were included. All 3 seemed to take origin in a pillar, either anterior or posterior, and where origin from other parts of the oropharynx or from outside the oropharynx was recorded as the primary site by the examining clinician, the lesions were excluded.

The minimum follow-up period was 27 months (2 cases). Taking a minimum of 3 years would have made 6 cases not available for analysis and altered the 27 month survival figures downwards by a mere 2 per cent. Nevertheless, 3 year end results have been used in some of the subgroups considered. Since only 1 patient in the whole group exhibited first recurrence after 18 months, a 27 month analysis was felt justified in order to admit these additional 6 patients. This pattern of early recurrence has been noted by other authors.[9,13] Indeed, some have taken periods as short as 13 months in analyzing results.[10]

Table II summarizes the distribution, lymph node involvement, and methods of treatment in the 41 cases. Of note is the relatively high incidence of clinically involved lymph nodes in this series.

TREATMENT

A. *Surgery*. The 2 cases treated by surgery alone were disease-free at 5 years. One of these had local removal of a lesion confined to the anterior pillar and the other had a T_2N_1 tumor of the fossa treated by

Table II

CARCINOMA OF TONSIL

ANALYSIS OF CELL TYPE, LYMPH NODE INVOLVEMENT AND TREATMENT METHODS

Type	No.	Clinical Lymph Node	Surgery	Radiation	Both
Squamous Cell Carcinoma	34	25	2	26	6
Lymphoepithelioma	7	7		6	1
Others	11				

Clinical Lymph Node Involvement in this Series 78%

Concannon[3]	44%	Rolander *et al.*[10]	40%
Fayos and Lampe[5]	53%	Scanlon *et al.*[11]	50%
Perez *et al.*[8,9]	61%		

partial pharyngectomy and ipsilateral block dissection.

B. *Radiation Alone.* Thirty-two cases were treated by biopsy and irradiation.

C. *Radiation plus Surgery.* Seven cases are classified as having been treated by both methods. In 4, this was done as a planned procedure, and in the other 3, surgery was used to salvage failed radiation cases. One of these cases had excisional biopsy of a lymph node outside the irradiated area only.

SURVIVAL

Table III presents the 3 and 5 year survivors in each group. It appears that the Radiation Alone cases did worst, and this major group was, therefore, analyzed in further detail.

ANALYSIS OF IRRADIATED CASES

Staging. Table IV presents the staging data on all 32 cases treated by irradiation alone. It will be seen that clinically positive lymph nodes were present in 79 per cent, which is no different from the series as a whole, and that 11 of the 13 disease-free survivors at 27 months had disease of Stage T_2N_1 or better. In keeping with our method of analysis, the other 19 cases are all considered as dead with recurrent or uncontrolled disease.

Twelve of these 19 had disease in the treated area.

Dosage. In order to further explore the reasons for radiation failure, it was first necessary to standardize the various methods of applying this radiation over the 20 year period. This was done by using the Nominal Standard Dose (N.S.D.) concept,[4] and expressing the results in tissue rets. It is realized that there may be controversy concerning the standardization in tissue, rather than tumor rets, but the purpose here was not to accurately define tumor effective dose by mathematical means so much as to classify the various treatments given around a well known standard.

An arbitrary figure of 1,700 rets (representing 4,950 rads in 20 treatments in 26 days) was used to divide the radiation cases. This figure was chosen for 2 reasons: (a) it represents what the authors hold to be adequate, well tolerated treatment in this disease, and does not preclude radical surgery; and (b) the highest dose in the "low" range was 1,637 rets, and the lowest dose in the "high" range was 1,713 rets. This gave a 76 ret difference, and prevented "marginal crowding" as would have happened had, say, 1,750 rets been taken as the standard.

In 1 case, the dosage was not known, leaving 31 cases available for analysis into "high" and "low" dose groups.

Recurrence. Table V presents the data on recurrence (including unresolved primary tumor) and the disease-free survivors at 27 months. The sole survivor in the "low" dose group was the patient who received the

TABLE III

CARCINOMA OF TONSIL
CRUDE DISEASE-FREE SURVIVAL RATES
AT 3 AND 5 YEARS

3 Years		5 Years	
Treatment	No.	Treatment	No.
Surgery	2/2	Surgery	2/2
Radiation	10/26	Radiation	7/24
Both	3/7	Both	3/7

TABLE IV

CARCINOMA OF TONSIL
IRRADIATED GROUPS BY STAGING, DISEASE-FREE
SURVIVAL AT 27 MONTH INTERVAL

	T_1	T_2	T_3	Totals
N_0	3/3	1/3	0/1	4/7
N_1	3/4	4/9	1/6	8/19
N_2	—	0/1	0/1	0/2
N_3	1/2	—	0/2	1/4
Totals	7/9	5/13	1/10	13/32

The number of survivors is represented over the total number of cases in each stage. The upper left hand corner of the diagram (heavy lines) indicates disease of Stage T_2N_1 or better.

TABLE V

CARCINOMA OF TONSIL
RELATIONSHIP OF ADEQUATE RADIATION DOSAGE TO RECURRENCE IN TREATED AREA

Less than 1,700 rets	More than 1,700 rets
8/13	4/18
Disease-Free (27 Months)	
Less than 1,700 rets	More than 1,700 rets
1/13	12/18

N.S.D. formula according to Ellis.[4] Minimum difference between 2 groups = 74 rets (*i.e.*, no case between 1,638 and 1,712 rets). N.S.D. (rets) = $D \times N^{0.24} \times T^{0.11}$.

highest dose in this range (1,637 rets). Moreover, one of the 4 failures in the "high" dose group received the lowest dose in the range (1,713 rets). The other 3 failures in the "high" dose group consisted of 2, who had uncontrolled primary disease evident within 1 month of completion of therapy, and 1 case who had metastases and presumed recurrent disease after a free period of 8 months. The 2 cases with uncontrolled primary disease received the highest doses in the series (2,200 rets).

All failures in the "low" dose group were evident from 1–18 months.

Staging of Recurrence. Obviously, it is not possible to draw any conclusions from data based on dosage alone, as more palliative therapy may have been used in the more advanced tumors. Accordingly, the 2 groups were subdivided as to stage to ascertain how important this influence was in the failures.

Table VI illustrates that the "low" dose group did, in fact, have worse disease than the "high" dose group. However, this alone does not explain the marked difference in outcome. If T_2N_1 (the commonest single stage) is used to divide the group, a breakdown of Staging / Dosage / Survival is possible (Table VII). It is readily seen that cases in the "high" dose group have a significantly increased advantage at all comparable stages. In fact, no patient in the "low" dose group is a 5 year survivor. The only survivor in this group has a 30 month disease-free period at the end of 1971.

RADIATION PLUS SURGERY

Of the 7 cases in this group, N.S.D. could not be calculated in 1 patient who had an implant. Two of the 3 survivors were in the "high" dose range, and the third received 1,679 rets and excision of a lymph node outside the irradiated area. In the 3 failures, "low" dose was used preoperatively and the surgery seemed to be inadequate to control the local failures. Once again, staging of the tumors in the 2

TABLE VI

CARCINOMA OF TONSIL
EFFECT OF LOW AND HIGH RADIATION DOSAGE RELATIVE TO STAGING OF THE PRIMARY LESION

	"High"				"Low"			
	T_1	T_2	T_3	Total	T_1	T_2	T_3	Total
N_0	3/3	1/2	0/1	4/6	—	0/1	—	0/1
N_1	2/2	4/5	1/3	7/10	1/2	0/3	0/3	1/8
N_2	—	—	0/1	0/1	—	0/1	—	0/1
N_3	1/1	—	—	1/1	0/1	—	0/2	0/3
Total	6/6	5/7	1/5	12/18	1/3	0/5	0/5	1/13

Note distribution of "T_2N_1 or better" disease in the 2 groups. Comparison of any single stage shows improved survival pattern in the "high dose" group.

groups could not explain the difference in outcome. When the 31 radiation cases and the 6 combined treatment cases are placed in Stage Categories and divided into "low" and "high" dose groups, it becomes apparent that the number of favorable cases in the "low" dose group has actually increased (Table VIII). The numbers are small, but the findings significant, as this is the experience with cancer in any site. Inadequate surgery added to inadequate irradiation is not likely to succeed. In like manner, inadequate irradiation is even less likely to salvage the failures of inadequate surgery.

Thus, of the 37 cases treated either by Radiation Alone or by Radiation plus Surgery, 16 were disease-free at 27 months minimum. Ten cases in the "low" dose group had disease of T_2N_1 or better, and the only 2 survivors in the whole group came from this 10, having received doses between 1,600–1,700 rets. In the "high" dose group, 13 cases had this favorable staging, and 11 were disease-free at 27 months. Three survivors had disease worse than T_2N_1, and they all came from the "high" dose group.

Table IX summarizes the data on the Radiation Alone and Radiation plus Surgery series at 27 months, 36 months, and 60 months. The percentages are age-adjusted only.

TABLE VII

CARCINOMA OF TONSIL
SURVIVAL RATES COMPARING HIGH AND LOW DOSAGE RADIATION IN T_2N_1 OR BETTER LESIONS AND WORSE THAN T_2N_1 LESIONS

	T_2N_1 or Better			Worse Than T_2N_1	
Dose	High	Low	Dose	High	Low
	10/12	1/6		2/6	0/7

INFLUENCE OF LYMPHOEPITHELIOMAS

There is a commonly held view that lymphoepitheliomas exert a favorable influence on radiation results in epidermoid carcinoma.

Four of the 7 lymphoepitheliomas in the series were 5 year survivors. These 4 cases are all present in the 27 month and 36 month analyses. This is not statistically different from the survival experience of the "high" dose group as a whole, but 1 of these survivors contributes the sole 5 year survivor in the "Low Dose plus Surgery" group. All 4 survivors had disease that was T_2N_1 or better.

INFLUENCE OF LYMPH NODE INVOLVEMENT

In the "high" dose group, 8 of the 12 cases with lymph node involvement were controlled. Six of these were N_1, and only 1

TABLE VIII

CARCINOMA OF TONSIL
27 MONTH SURVIVAL RATES COMPARING HIGH AND LOW DOSAGES IN 37 CASES RECEIVING RADIATION

	High Dose				Low Dose			
	T_1	T_2	T_3	Total	T_1	T_2	T_3	Total
N_0	3/3	1/2	0/1	4/6	—	0/2	—	0/2
N_1	3/3	4/5	2/4	9/12	1/2	1/6	0/3	2/11
N_2	—	—	0/1	0/1	—	0/1	—	0/1
N_3	1/1	—	—	1/1	0/1	—	0/2	0/3
Total	7/7	5/7	2/6	14/20	1/3	1/9	0/5	2/17

Favorable disease exhibited in top left hand corners (heavy lines).

TABLE IX

CARCINOMA OF TONSIL
DISEASE-FREE SURVIVAL (AGE-ADJUSTED)
IN THE TREATMENT SUBGROUPS

Treatment	27 mo.	36 mo.	60 mo.
"High Dose" Radiation	71 %	69%	68.1%
"Low Dose" Radiation	9.3%	—	—
"High Dose" plus Surgery	—	—	72.6%
"Low Dose" plus Surgery	—	—	9 %
All Radiation Alone	43.8%	42%	31.6%

Note similarity of results at the 3 periods in the "high dose" group.

of the 12 cases had N_2 (bilateral) disease. Perez *et al.*[8,9] reported only 13 responders of 42 with lymph node disease. Ten of their 42 cases, however, had bilateral involvement and if the T_2N_1 cases only are considered, they achieve control in 11 of 15 cases. Schulz[13] reported control of lymph node disease in 52 per cent of cases treated with more than 5,000 rads in 5 weeks, compared with control in only 20 per cent treated at lower dosage.

CARCINOMA OF THE NASOPHARYNX

This series comprised 72 cases, of whom 4 received no treatment and 1 received treatment outside the Province. All 72 were admitted to the study, and Table x presents crude survival rates.

Of the 27 lymphoepitheliomas, 7 exhibited recurrence in the treated area, and of the 45 S.C.C.s, 25 had local recurrence. This is a higher rate of recurrence than in Chen and Fletcher's series[2] or the earlier series of Fletcher and Million.[6] Six of the 32 recurrences in the present series occurred after 2 years.

Lymph node involvement was present in 83 per cent of the epidermoid carcinomas in this region.

ANALYSIS OF FAILURES

Once again, the concept of N.S.D. was used, and once again 1,700 rets was taken as the dividing line between "high" and "low" dose. This is not considered a satisfactory dose for nasopharyngeal cancer, but taking a higher N.S.D. made the "high" and "low" dose groups grossly unbalanced, and did not, in fact, influence the data to be presented to any great extent.

The clinical Stage T_2N_1 was used to divide the series.

Table xi shows the effect of dosage on the end results for the 2 histologic types. The "high" dose group seems to have produced better results than the "low" dose group, but the difference is not as marked as in tonsillar cancer. In S.C.C., for instance, 3 of the 7 survivors at 5 years came from the "low" dose group, and in the lymphoepitheliomas, 3 of the 5 survivors at 5 years came from the "low" dose group. "Low" dose, however, was used in over 75 per cent of the cases available for 5 year analysis.

When the effect of staging is taken into consideration (Table xii), further information on the causes of failure becomes available.

The 5 lymphoepithelioma patients, who survived 5 years (Table xiii), comprised 4 with disease T_2N_1 or better. Two of these came from the "high" dose group, and 2 from the "low" dose group. The other survivor had worse disease and low dosage.

The 7 cases of S.C.C., who survived 5 years, all had disease of T_1N_0 or T_1N_1. No case with disease T_2N_1 or worse survived 5 years. However, only 6 cases received doses in excess of 1,800 rets, and 2 of these were disease-free at the 5 year period.

TABLE X

CARCINOMA OF NASOPHARYNX
INCIDENCE OF CELL TYPES, NODAL INVOLVEMENT,
AND CRUDE 2 AND 5 YEAR SURVIVAL RATES

Type	No.	Lymph nodes positive	2 yr.	5 yr.
Squamous Cell Carcinoma	45	39	12/45	7/34
Lympho-epitheliomas	27	21	14/27	5/18
Others	13	—	—	—

Clinically positive lymph nodes were present in 60 of 72 epidermoid carcinomas (83 per cent).

Analysis of the N.S.D. showed no hint of consistency with regard to local recurrence, especially in the S.C.C.s. One "high" dose S.C.C. and one "low" dose lymphoepithelioma have recurred after a free interval of 5 years.

DISCUSSION

The 2 sites of tonsil and nasopharynx (Tables XIV and XV) were chosen because they present similar pathology and because there appeared, superficially, to be little difference in the end-results obtained at both sites. At the 5 year period 7 of 24 (29 per cent) cases with tonsillar carcinoma and 12 of 52 (23 per cent) cases with nasopharyngeal carcinoma, treated by radiation alone, were free of disease. However, when the sites are further analyzed, it is found that there are quite marked differences in the behavior and curability of these lesions.

Of 12 "primary" failures in tonsillar cancer, only 1 occurred after 18 months. These failures are almost certainly the direct result of inadequate therapy rather than advanced disease, although the latter, of course, is generally of poor prognostic significance. An N.S.D. of 1,700 rets was used to divide all irradiated lesions into "high" and "low" dose groups. In cancer of the tonsil, a good positive correlation between dosage, tumor clearance, and patient survival is shown. In the present material, an over-all clearance rate of 72 per cent for all stages was achieved with doses higher than 1,700 rets. This correlates well with some other series where a similar dosage was most probably given—Concannon[3] 70 per cent, Perez *et al.*[9] 60 per cent and Schulz[13] 78 per cent. It should be stressed, however, that the relationship is not a straight exponential one. Two of the 4 failures in the "high" dose group received 2,200 rets, and the 1 survivor in the "low" dose group received 1,637 rets. This fortifies the clinical impression that some tumors are innately radioresistant and that even high doses of radiation, by conventional methods, will fail to achieve control.

It is interesting to note that of 7 patients treated with adequate dosage since the beginning of 1967, only 1 case has recurred within the irradiated area. This was a T_3N_0 lesion.

These failures should be treated by radical surgery, if this is possible, and if the dose has been kept within tolerance limits of 1,700–1,750 rets, local factors will not preclude this. There is little point in increasing the dosage applied over the range suggested, as this will merely contribute more morbidity and postsurgical complications in this type of case. Therefore, it is suggested that all patients who

TABLE XI

SQUAMOUS CELL CARCINOMA AND LYMPHOEPITHELIOMA OF NASOPHARYNX
EFFECT ON SURVIVAL RATES OF HIGH AND LOW DOSAGE RADIATION THERAPY

Squamous Cell Carcinoma	Lymphoepithelioma
High Dose	*High Dose*
5/11 at 2 yr.	5/7 at 2 yr.
4/7 at 5 yr.	2/4 at 5 yr.
Low Dose	*Low Dose*
7/29 at 2 yr.	9/20 at 2 yr.
3/22 at 5 yr.	3/14 at 5 yr.

Five cases of squamous cell carcinoma not treated.

TABLE XII

SQUAMOUS CELL CARCINOMA AND LYMPHOEPITHELIOMA OF NASOPHARYNX
INFLUENCE OF STAGING ON SURVIVAL RATES

2 Yr. Disease-Free

	T_2N_1 or better	Worse than T_2N_1
Squamous Cell Carcinoma	9/24	3/21
Lymphoepithelioma	12/19	2/8

5 Yr. Disease-Free

	T_2N_1 or better	Worse than T_2N_1
Squamous Cell Carcinoma	7/18	0/16
Lymphoepithelioma	3/10	2/8

TABLE XIII

SQUAMOUS CELL CARCINOMA AND LYMPHOEPITHELIOMA OF NASOPHARYNX

5 YEAR AGE-ADJUSTED SURVIVAL RATES

Squamous Cell Carcinoma	7/34	21.6%
Lymphoepithelioma	5/18	28.8%

All 7 squamous cell carcinoma survivors had early tumors; 3/5 lymphoepithelioma survivors had early tumors.

have received adequate irradiation and have persistent tumor 6 weeks following completion of therapy be re-assessed for surgery. However, inadequate surgery added to inadequate irradiation is a poor combination.

Rolander *et al.*[10] reported 9 of 15 patients with T_3 lesions as survivors following planned preoperative irradiation plus surgery. Their N.S.D. was probably between 1,500 and 1,600 rets, but the patients had radical surgery performed which encompassed all the area originally known to be occupied by tumor.

All but 1 of the recurrences in this series occurred within 18 months, and Table IX reflects this, in that the disease-free survival figures at 27 months, 36 months, and 5 years are virtually the same in the adequately treated patients. For disease T_2N_1 or better, the "high" dose group has a 27 month disease-free survival of 83 per cent. Perez *et al.*[9] show 73 per cent 5 year survivors in this group, but their staging system allows 4 categories of "T."

In fact, comparison with other series is difficult because of the variety of staging methods employed, differing methods of adjusting crude survival rates, and the variability of radiation techniques and dosage in different centers. The methods of calculating results vary considerably in published series. Once again, it is stressed that in this series, all cases not free of disease are considered as dying of disease. Treatment mortality is a rare complication of radiation therapy, but an important factor in the surgical series. In our opinion the morbidity associated with radical surgery is acceptable in uncontrolled disease, but is not otherwise justified.

In the case of nasopharyngeal carcinoma, however, the picture is not as clear. The results in this material are poor, and it is felt that this is probably the experience of most centers in treating this type of cancer. Some authors[2,12] have reported much better survivals with somewhat different treatment regimens. Chen and Fletcher[2] have analyzed their material on the basis of N.S.D. and had the same unpredictable results with squamous cell carcinomas. Recurrences in the present series were unpredictable in both types of tumor. One S.C.C. and 1 lymphoepithelioma recurred more than 5 years after treatment. As already mentioned, staging in this site was sometimes difficult. Although all patients have tomography at the present time, many in this series did not.

We believe that higher dosage in the lymphoepithelioma group would have produced a better survival experience. Perhaps the same holds true for the squamous cell carcinomas. The fact remains that the stage of the disease seemed to be all important. This is not to deny the place of radical therapy in cancer of the nasopharynx. Unless a decision is taken to

TABLE XIV

SUMMARY—CARCINOMA OF THE TONSIL

1. Radiation therapy is the preferred method of treatment
2. Radical radiation therapy leads to a high percentage of cures
3. Extremely high doses are not necessary for control
4. Failures to radiation therapy tend to occur early
5. When failure is evident, radical surgery should be undertaken without hesitation in operable cases

TABLE XV

SUMMARY—CARCINOMA OF THE NASOPHARYNX

1. Of the 12 5 year survivors, 10 were of early stage
2. In squamous cell carcinoma, staging appeared to be much more relevant to the outcome than dosage
3. In lymphoepithelioma, dosage may be just as important as staging in the ultimate prognosis

treat palliatively because of very advanced disease, N.S.D.s of at least 1,750 rets should be used. Unfortunately, surgical salvage is rarely possible and it appears, in this series, that improved results have only been obtained by diagnosing the disease in early stages, and treating these cases, at least, with adequate therapy.

SUMMARY

Carcinoma of the tonsil, especially with comparatively early disease, is a highly curable condition, when adequate irradiation is used. Failure to achieve control becomes evident early. If the primary tumor is still present 6 weeks following completion of therapy, radical surgery should be considered and should include all of the original area involved by tumor. Clearance of primary tumor with persistence of lymph node disease following adequate therapy is probably an indication for neck dissection alone. Obviously, involvement of both surgeon and radiotherapist in the initial assessment and at follow-up is highly desirable.

Universal application of one staging system, one method of adjusting crude survival, and one expression of radiation dosage should be encouraged.

In carcinoma of the nasopharynx, the U.I.C.C. method of staging proved difficult to apply retrospectively. However, it was possible to define and stage early disease, and these cases provided most of the survivors. The pattern of recurrence related to dose was unpredictable.

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LARYNGEAL CARCINOMA: CORRELATION OF ROENTGENOGRAPHY AND HISTOPATHOLOGY*

A STUDY BASED ON WHOLE ORGAN, SERIALLY SECTIONED LARYNGEAL CARCINOMA SPECIMENS

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DIAGNOSTIC radiologic examinations, that is plain roentgenograms, tomograms and laryngograms, are considered a prerequisite for the accurate assessment and management of laryngeal carcinoma. In 1899 and in 1901 Scheier[34,35] was one of the first to report his studies of the larynx by roentgen examinations. He studied the ossification of the laryngeal cartilages on autopsy specimens. The exposure time was so long that it was difficult to use the method on living subjects. In 1903, Möller and Fischer[26] used roentgen rays to study the function of the cricothyroid muscle. In 1913 Thost[39] made the first attempt to study the pathology of the larynx by roentgen examinations. In 1914 Iglauer[12] pointed out the value of roentgenography in the diagnosis of diseases of the larynx and the trachea. In 1922 Coutard[3] emphasized that the roentgenologic examination should be added to the other examination methods of the larynx before the mode of treatment was decided. In 1934 Worning[42] and in 1938 Baclesse[2] made additional contributions to the laryngeal radiology.

Tomography. In 1937 Gunsett,[5] and in 1940 Leborgne,[20] described the tomography technique for larynx, which has markedly improved the accuracy of assessment of laryngeal carcinomas. In combination with the clinical examination including palpation, indirect laryngoscopy (mirror), and direct laryngoscopy, tomography has been one of the most valuable methods for the clinician in the assessment of laryngeal tumors. A number of different tomographic techniques have been described.[1,23,37]

Contrast Laryngography. In 1926 Iglauer[13] used iodized oil for visualization of subglottic stenosis. In 1936 Jackson[14] described a method of coating the laryngeal mucosa with a radiopaque material. Lindgren[23] used a similar technique. Popularization of the techniques, however, occurred only after 1957, when Powers *et al.*[33] illustrated and emphasized the value of this technique. In many centers the technique is still not used or less frequently used than the tomography technique. Laryngography when used in combination with tomography does, however, give a better assessment of the laryngeal ventricles and of the piriform fossae. The lateral view reveals the posterior surface of the epiglottis and the technique is also of particular value in assessing involvement of the anterior commissure. When contemplating horizontal partial laryngectomy, the assessment of ventricular involvement and of subglottic extension at the anterior commissure is of particular importance and this is best done with laryngography. Many authors have shown that laryngography is an important aid in the staging and treatment of laryngeal carcinoma.[9,28,30–33] Different techniques have been discussed.[6,10,18,19,21,25,29,38]

Whole Organ Laryngeal Sectioning. Sectioning of the whole organ laryngeal carcinoma specimen with comparison of the clinical, roentgenologic and pathologic examinations was first described by Leroux-Robert in 1936.[22] The serial sectioning technique was not widely used until the 1950s,[15] and relatively few centers are using it at the present time.[7,8,16,27,40,41] A modified paraffin

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embedding technique was developed at the M. D. Anderson Hospital[24] and has been more recently used at the Armed Forces Institute of Pathology in Washington.[11] A comparison of tomograms and serially sectioned laryngectomy specimens is illustrated in MacComb and Fletcher's text book on Cancer of the Head and Neck.[24] Earlier work done at the same center in 1954 correlated the preoperative tomograms with thick slices from the decalcified laryngectomy specimens.[4]

Whole organ serial sectioning of laryngeal carcinoma surgical specimens has been performed in our center since 1966. In the past year we have attempted to correlate the roentgenologic assessment with the histopathologic findings in the resected specimens. This has been done in an effort to improve our knowledge, and also to reveal the limitations and the diagnostic possibilities of the various roentgenographic techniques.

MATERIAL AND METHOD

Since 1966 we have collected 115 laryngectomy specimens from patients with laryngeal carcinoma, in which we have serially sectioned the whole larynx. From the large number of preoperative laryngograms and tomograms that have been obtained on these patients, 10 cases have been selected to illustrate the strengths and weaknesses of the various roentgenographic techniques employed. At the present time the laryngeal specimens are paraffin embedded and subserially sectioned at 1 mm. levels. The sectioning has been done in the coronal plane in most instances to be able to correlate the histopathologic findings with the roentgenographic studies.

At the present time we employ the following roentgenographic techniques in a routine manner preoperatively: An upright lateral plane roentgenogram of the larynx is taken to show the air column, soft tissues and cartilaginous structures. Following this, anteroposterior tomography is done in the supine position at 5 mm. intervals. These intervals are measured from the thyroid notch anteriorly. Tomography at a specific level is then routinely performed during the various laryngeal maneuvers (phonation, Valsalva maneuver, and reverse Valsalva maneuver). In those instances where it appears that the anterior commissure is involved by tumor, lateral tomography is also employed.

Following this, laryngography is performed using the method described by Landman.[18] Hytrast (iopydone-iopydol) is used as the contrast medium. This is introduced either orally or through a nasal tube. Upright spot roentgenograms are taken in the straight anteroposterior view and a straight lateral view and then repeated during the various laryngeal maneuvers. In special cases cineroentgenography is used to provide information of the mobility of the vocal cords. The final procedure of the examination is overhead roentgenograms in the straight anteroposterior and lateral views.

ILLUSTRATIVE CASES

Case I. (Fig. 1, *A* and *B*) Mr. A.R., aged 52 years, smoked 20 cigarettes daily. Hoarseness for 2 years.

Laryngoscopy. Tumor involving the glottic and subglottic regions with involvement of the ventricle on the right side.

Tomography. Tumor occupying mainly the right vocal cord, but with slight subglottic extension and obliteration of the ventricle.

Treatment. Tracheotomy for airway obstruction followed by total laryngectomy and radical neck dissection.

Pathology. Glottic tumor extending subglottically beneath the conus elasticus and also extending around the laryngeal ventricle to the false cord in the middle portion of the cord.

Comment. The histopathologic findings as to the mucosal extent of tumor growth correlate reasonably well with the tomograms and the clinical assessment. The depth of invasion is not accurately assessable either by clinical means or by the use of tomography. The clinical finding of mobile vocal cords confirmed by tomography is, however, suggestive evidence that the tumor growth is rather superficial.

Case II. (Fig. 2, *A* and *B*) Mr. F.K., aged 74 years, smoked 20 cigarettes per day. Tumor of the right vocal cord irradiated with 5,500 rads

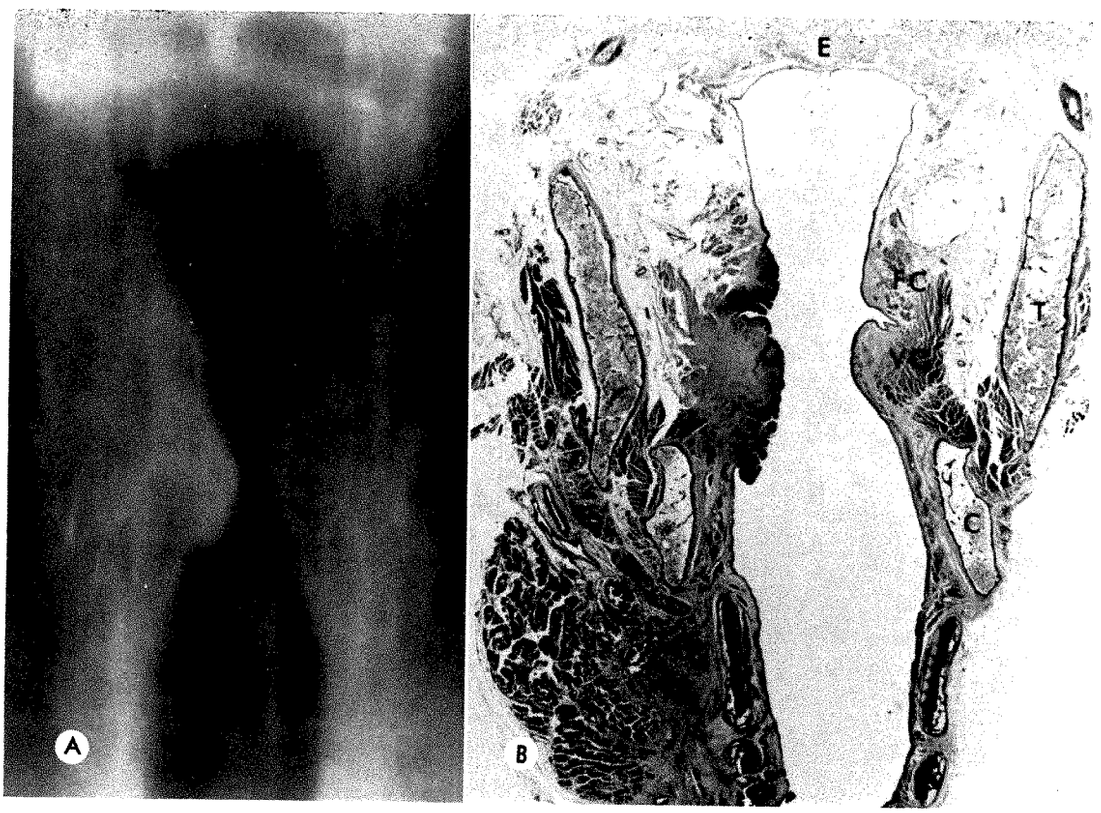


FIG. 1. Case 1. (*A*) Tomogram and (*B*) coronal section of a larynx at the level of middle third of the vocal cords. There is a carcinoma of the right vocal cord with spread subglottically and extension around the ventricle into the false cord ("transglottic" distribution). Note the excellent correlation between the tomogram and the histologic section. C = cricoid; E = epiglottis; FC = false cord; T = thyroid ala; VC = vocal cord.

Co^{60} teletherapy. Four years later recurrent tumor.

Laryngoscopy. Tumor of right vocal cord with no subglottic extension.

Tomography. Deformity of the right vocal cord and obliteration of the right angled subglottic space. Compare the normal left side with the abnormal right side. Interpretation: Glottic tumor with subglottic extension.

Treatment. Total laryngectomy.

Pathology. There is an ulcerated tumor mass occupying the full length of the right vocal cord with subglottic extension. The upper portion of the cricoid cartilage is invaded.

Comment. This case illustrates the difficulty in assessing the vertical extension of glottic tumors when examined by laryngoscopy. There is a very good correlation between the tomogram and the surgical specimen. The depth of tumor invasion was not assessable in the tomographic study, nor was the invasion of the cricoid cartilage demonstrable.

CASE III. (Fig. 3, *A* and *B*) Mr. M.H., aged 57 years, pipe smoker since the age of 14 years, complained of hoarseness for 9 months. He was thought to have a glottic tumor occupying both vocal cords and was irradiated with 5,500 rads of Co^{60} teletherapy. Five months later residual disease was noted.

Laryngoscopy. Tumor occupying the anterior portion of the left vocal cord with impaired mobility and diffuse reddening of the right vocal cord.

Tomography. Symmetric swelling and obliteration of the right angled subglottic space bilaterally. Slight deformity of the right laryngeal ventricle. Interpretation: Subglottic circumferential tumor extension.

Treatment. Laryngectomy and left neck dissection.

Pathology. There is a primary subglottic tumor mass occupying the whole subglottic region from the cricothyroid membrane anteriorly to the posterior commissure. The tumor has

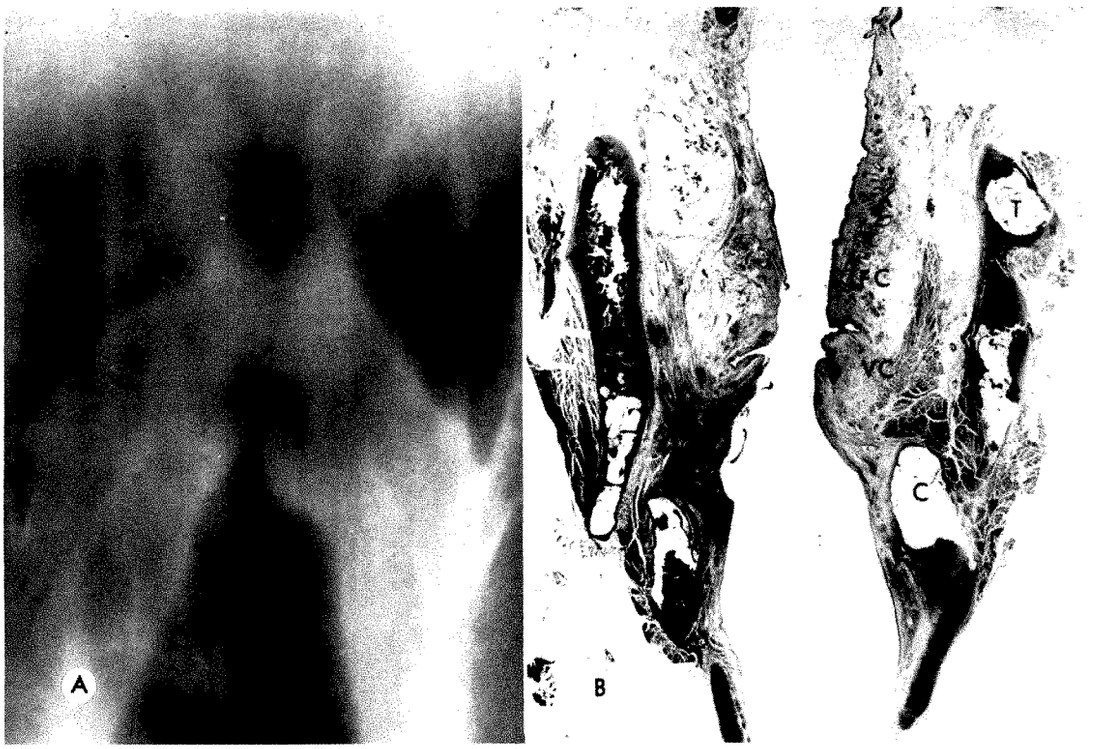


FIG. 2. Case II. (*A*) Tomogram and (*B*) coronal section of a larynx at the level of the middle third of the vocal cords just anterior to the vocal process. There is a large carcinoma of the right vocal cord with subglottic extension. This tumor has produced flattening of the subglottic angle in the tomogram. C = cricoid; FC = false cord; T = thyroid ala; VC = vocal cord.

spread beneath the lower margin of the cricoid bilaterally with invasion of the cricoid cartilage.

Comment. This case illustrates the difficulty in assessing the vertical extension of tumors by laryngoscopic examination. The impaired mobility of the right vocal cord is explained by extension of the tumor to the postcricoid region below the cricoid with invasion of the posterior cricoarytenoid muscle on the right side. Here again the tomograms correlated very well with the pathologic specimen. The invasion of the cricoid cartilage and extension of tumor outside the laryngeal framework was not assessable by the tomograms.

CASE IV. (Fig. 4, *A–D*) Mr. F.M., aged 60 years, smoked 20 cigarettes per day all his adult life. He complained of hoarseness of 9 months' duration and shortness of breath for 2 months.

Laryngoscopy. Large tumor mass occupying the right vocal cord with extension subglottically and supraglottically. Right vocal cord fixed. Marked obstruction of his airway.

Tomography. Large tumor mass occupying the right side of the larynx with probable destruction of thyroid ala and cricoid cartilage. Large subglottic extension.

Laryngography. Piriform fossa filled well, suggesting no involvement of the piriform sinus.

Treatment. Irradiation with 500 rads followed by total laryngectomy and right neck dissection within 24 hours.

Pathology. Large glottic tumor on the right side with extensive supraglottic and subglottic extension. Destruction of the thyroid ala, cricoid cartilage and arytenoid cartilage. The tumor spread outside the larynx through the cricothyroid space.

Comment. Both the clinical assessment and the roentgenographic studies correlated very well with the pathologic specimen. The laryngogram suggested correctly that the piriform sinus was not involved by the tumor. Although the tomographic studies did suggest destruction of the laryngeal framework, the true depth of penetration of the tumor was not accurately

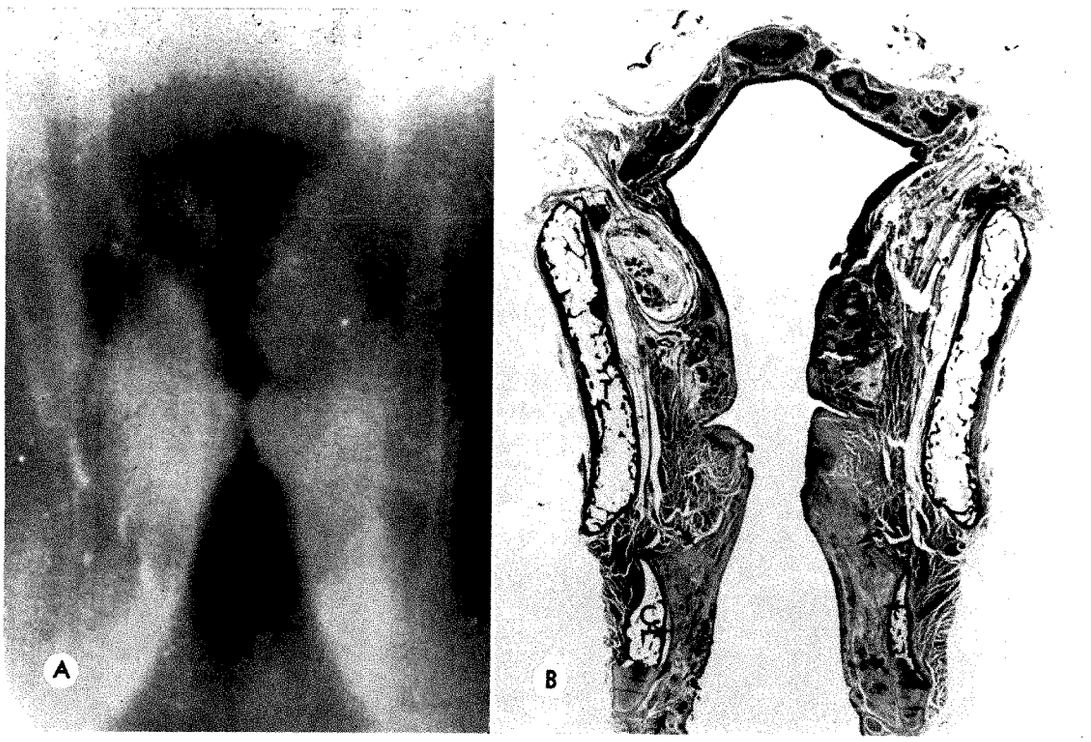


FIG. 3. Case III. (*A*) Tomogram and (*B*) coronal section of a larynx at the level of the vocal process of the arytenoid. There is a primary circumferential subglottic carcinoma (arrows). Note the bilateral obliteration of the subglottic angle in the tomogram (compare with Fig. 2). C = cricoid; T = thyroid ala.

assessable. The fixation of the vocal cord would also suggest deep invasion.

CASE V. (Fig. 5, *A* and *B*) Mr. W.B., aged 58 years, smoked 20 cigarettes per day. He complained of hoarseness of 7 months' duration. He received 5,500 rads of Co^{60} teletherapy for a small glottic tumor overlying the right vocal process. Six months later he had a right hemilaryngectomy for residual or recurrent tumor. The hemilaryngectomy specimen showed tumor occupying the posterior angle of the laryngeal ventricle and overlying the anterior and medial aspect of the right arytenoid. One year later he was again noted to have recurrent tumor on the right side of his larynx.

Laryngography. Roentgenographic studies were extremely difficult to interpret because of the previous partial laryngectomy. The left side was normal, but the right side was nodular and irregular throughout the whole of the hemilarynx.

Treatment. Total laryngectomy and right neck dissection.

Pathology. Very large tumor mass occupying the whole of the right hemilarynx. A separate 2×2 cm. tumor mass is present in the subhyoid region, probably an implantation tumor mass at the time of the previous surgical procedure.

Comment. This case illustrates that baseline tomograms should be taken following partial laryngectomy in order to better interpret future roentgenographic studies to assess recurrent disease. The baseline tomogram should be taken after the postoperative edema has subsided. The laryngeal tumor mass actually correlates very well with the tomographic study. The true depth of the tumor extension was not assessable, nor was the separate subhyoid tumor mass noted in roentgenographic studies.

CASE VI. (Fig. 6, *A* and *B*) Mr. G.McN., aged 49 years, smoked 40 cigarettes per day. He complained of pain at the base of his tongue of 1 year's duration.

Laryngoscopy. Large epiglottic tumor mass with destruction of the bulk of the epiglottis and extension to the right aryepiglottic fold.

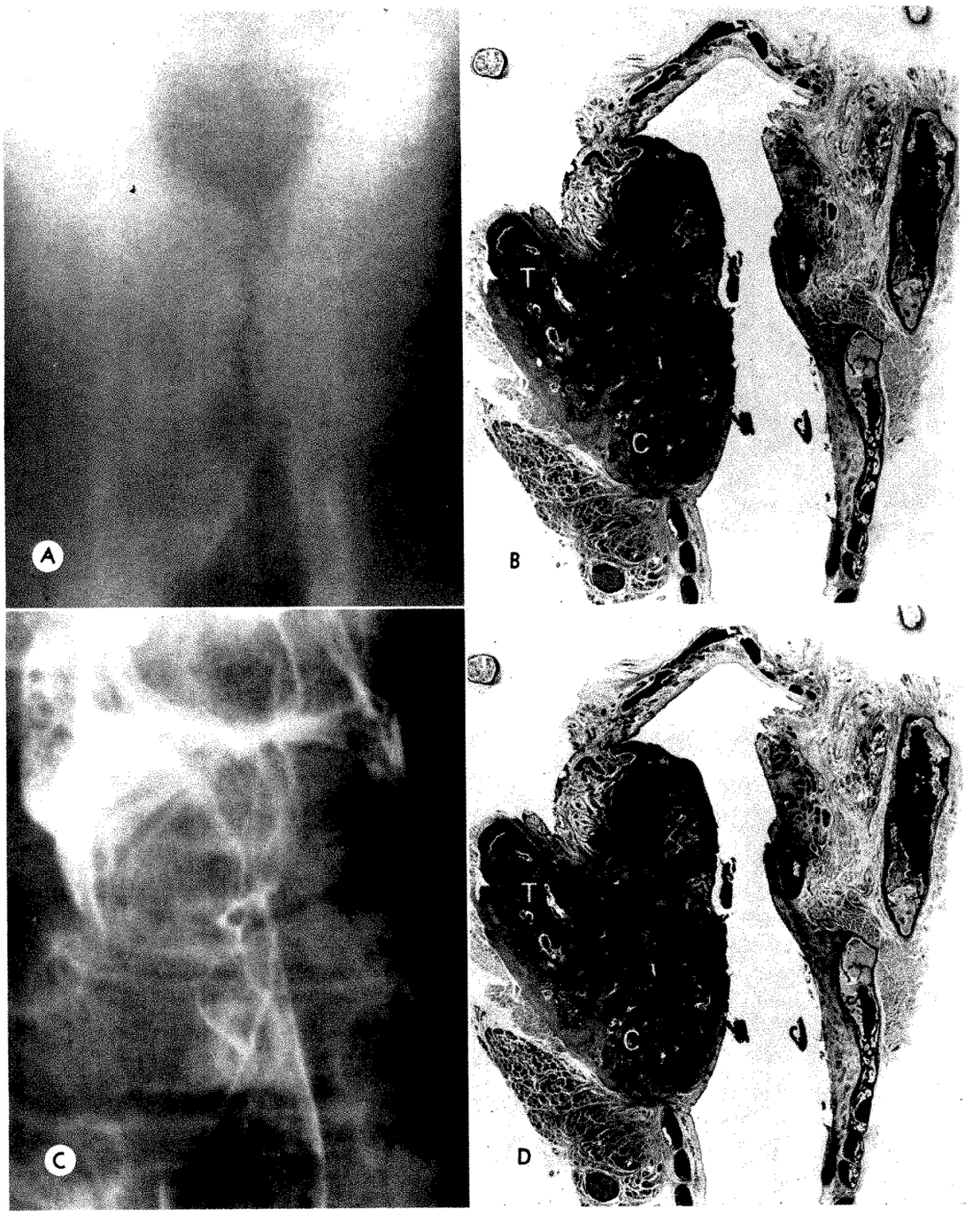


Fig. 4. Case IV. (*A*) Tomogram and (*B* and *D*) coronal sections of a larynx at the level of the posterior third of the vocal cords. (*C*) Laryngogram for the same case. There is a huge carcinoma of the right hemilarynx, with cartilage displacement and destruction. The endolaryngeal configuration of the tumor is well illustrated by the tomogram and laryngogram. The cartilage destruction and the extension of the tumor outside the larynx could not be assessed roentgenologically. C = cricoid; T = thyroid ala.

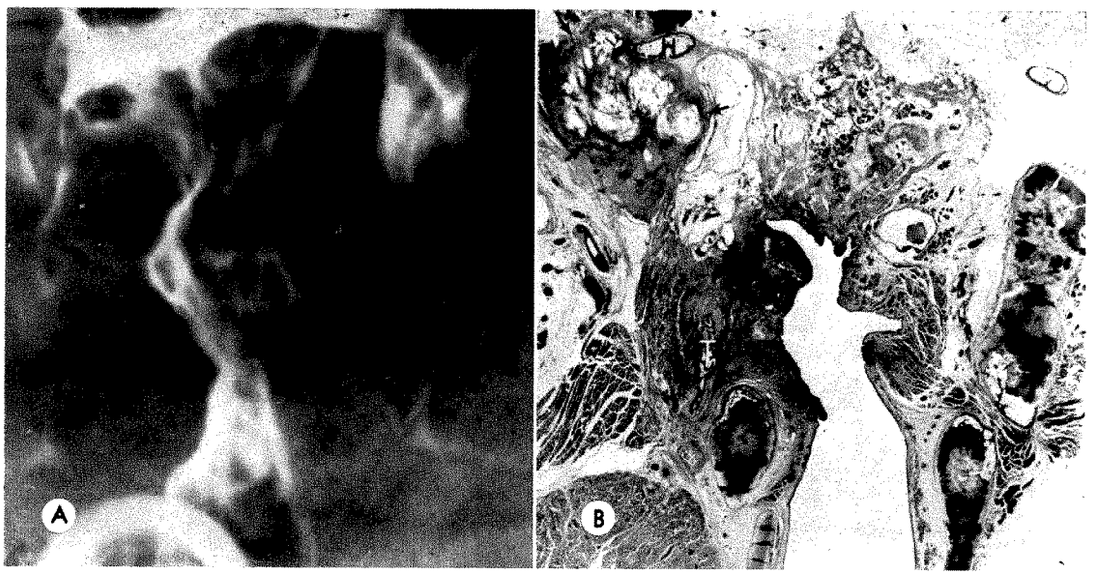


FIG. 5. Case v. (*A*) Laryngogram and (*B*) coronal section of a larynx taken at the level of the middle third of the vocal cords (previous right vertical hemilaryngectomy). There is a large carcinoma occupying the right hemilarynx. Note the separate tumor mass in the subhyoid region (arrows). H = hyoid bone; T = thyroid ala.

Valleculae clear; 1.5 cm. of normal mucosa separates the tumor from the anterior commissure.

Laryngography. Laryngograms confirmed the clinical findings.

Treatment. Supraglottic horizontal partial laryngectomy.

Pathology. Large tumor mass invading and destroying most of the right side of the epiglottis and extending to the right aryepiglottic fold. Much of the epiglottic cartilage has been destroyed by the tumor which penetrates through the cartilage to the submucosa of the valleculae; 1.5 cm. of normal mucosa separates the tumor from the anterior commissure.

Comment. Both the clinical assessment and the laryngogram correlate extremely well with the surface extension of the tumor as seen in the histologic sections. Of particular importance is the accurate assessment of the caudal extension of the tumor when performing horizontal supraglottic partial laryngectomy. It is impossible to assess cartilaginous destruction.

CASE VII. (Fig. 7, *A* and *B*) Mr. D.P., aged 73 years, smoked 20–25 cigarettes per day. He complained of recurrent hoarseness for many years. He was assessed as having a small glottic tumor of the right vocal cord and received 5,500 rads of Co^{60} teletherapy. Two years later he was found to have recurrent tumor.

Laryngoscopy. The tumor extended from the anterior commissure to the vocal process region of the right vocal cord (the anterior $\frac{2}{3}$ of the right vocal cord).

Tomography. Assessed as normal.

Treatment. Right hemilaryngectomy.

Pathology. Moderately well differentiated squamous cell carcinoma involving the anterior $\frac{2}{3}$ of the right vocal cord. No invasion of the anterior commissure was present and the arytenoid region was free of tumor.

Comment. Slight irregularity of the right vocal cord can be seen in the tomogram in retrospect. Small tumors occupying the free margins of the vocal cord with slight exophytic growth are difficult to assess by roentgenographic means. In this case the findings at laryngoscopy correlated extremely well with the findings in the pathologic specimen.

CASE VIII. (Fig. 8, *A* and *B*) Mr. E.S., aged 70 years. Smoking history unknown. He complained of hoarseness, lump in the throat and recurrent dyspnea for 2 to 3 months.

Laryngoscopy. A large tumor mass involving the left aryepiglottic fold.

Laryngography. Large tumor involving epi-

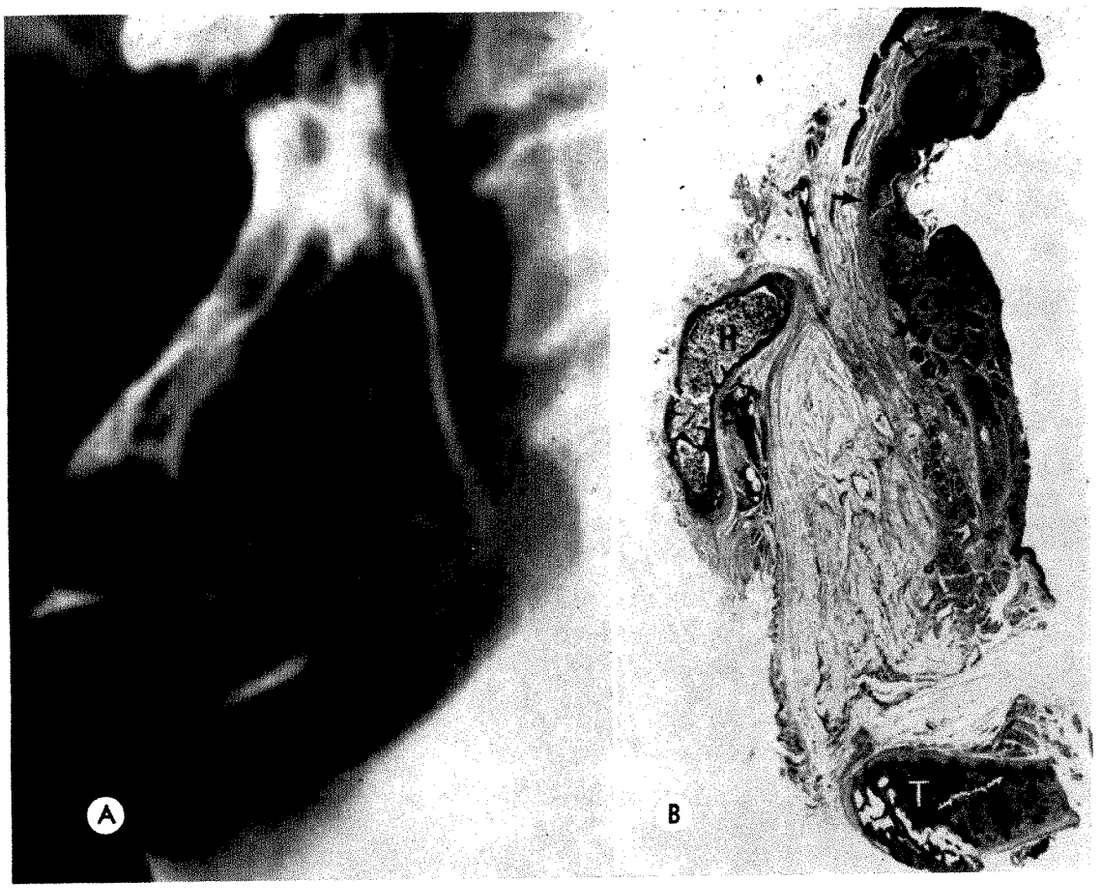


Fig. 6. Case vi. (*A*) Laryngogram and (*B*) midline sagittal section of a larynx. Note the irregular mucosal lining of the laryngeal surface of the epiglottis in the laryngogram, and the good correlation with the ulcerated tumor mass (arrows) of the epiglottis in the histologic section. H = hyoid bone; T = thyroid ala.

glottis, left aryepiglottic fold and left false vocal cord.

Treatment. Irradiation with 500 rads, followed by total laryngectomy and left neck dissection within 24 hours.

Pathology. Large supraglottic tumor involving the base of the epiglottis, both false vocal cords and both aryepiglottic folds. The tumor invades, partially destroys and penetrates the epiglottic cartilage with extension into the soft tissues of the submucosa of the vallecula. The tumor penetrates through the anterior portion of the thyroid ala and extends outside the laryngeal framework.

Comment. Here again there is good correlation between the roentgenographic studies and the surface extension of the tumor. The destruction of the epiglottic and thyroid cartilages was, however, not noted and it was impossible to assess the extension of the tumor into the submucosa of the vallecula and outside of the laryngeal framework.

Case ix. (Fig. 9, *A* and *B*) Mr. R.H., aged 55 years. Smoking history unknown. He complained of hoarseness, sore throat and dysphagia of 6 months' duration.

Laryngoscopy. Tumor mass involving the right arytenoid, right aryepiglottic fold, and right false vocal cord with extension to the medial wall of the right piriform fossa. There was no involvement of the vocal cords.

Tomography. Confirmed the laryngoscopy findings.

Treatment. Horizontal supraglottic partial laryngectomy and right neck dissection.

Pathology. Tumor of the right aryepiglottic fold extending from the epiglottis to the arytenoid. No invasion of the laryngeal cartilages. The tumor had extended over the top

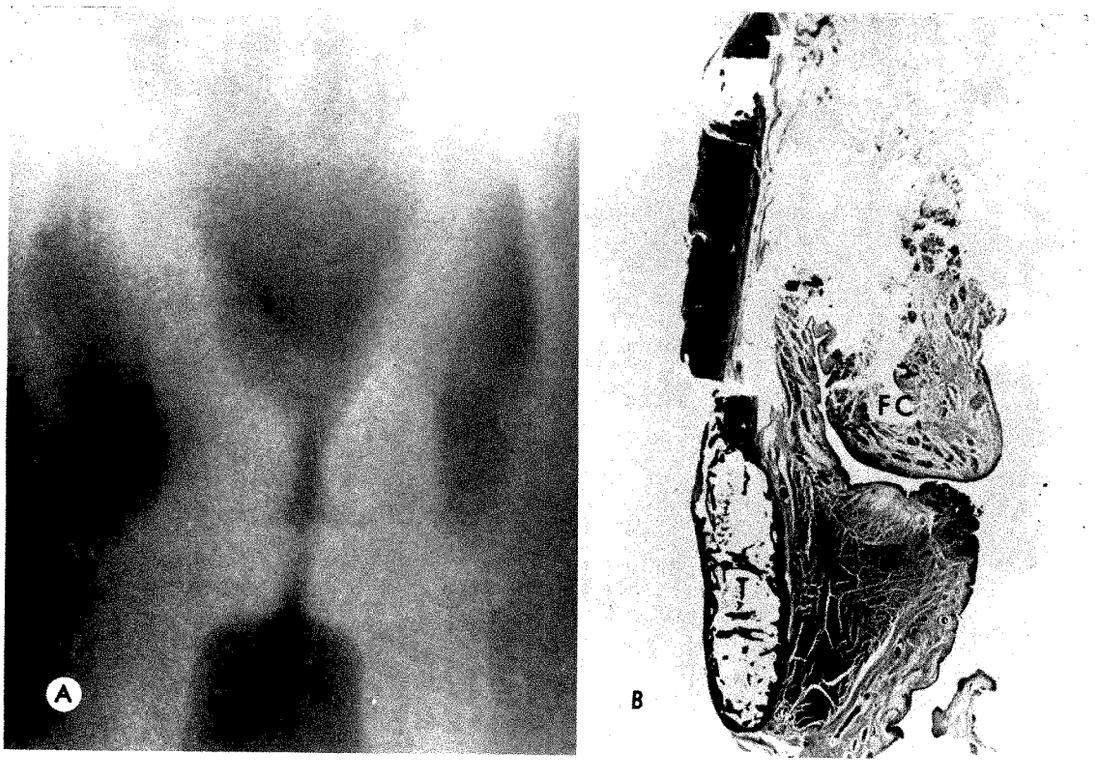


FIG. 7. Case VII. (*A*) Tomogram of a larynx showing no abnormality, and (*B*) coronal section of the partial laryngectomy specimen, revealing a small carcinoma of the free margin of the vocal cord (VC). FC = false cord; T = thyroid ala; VC = vocal cord.

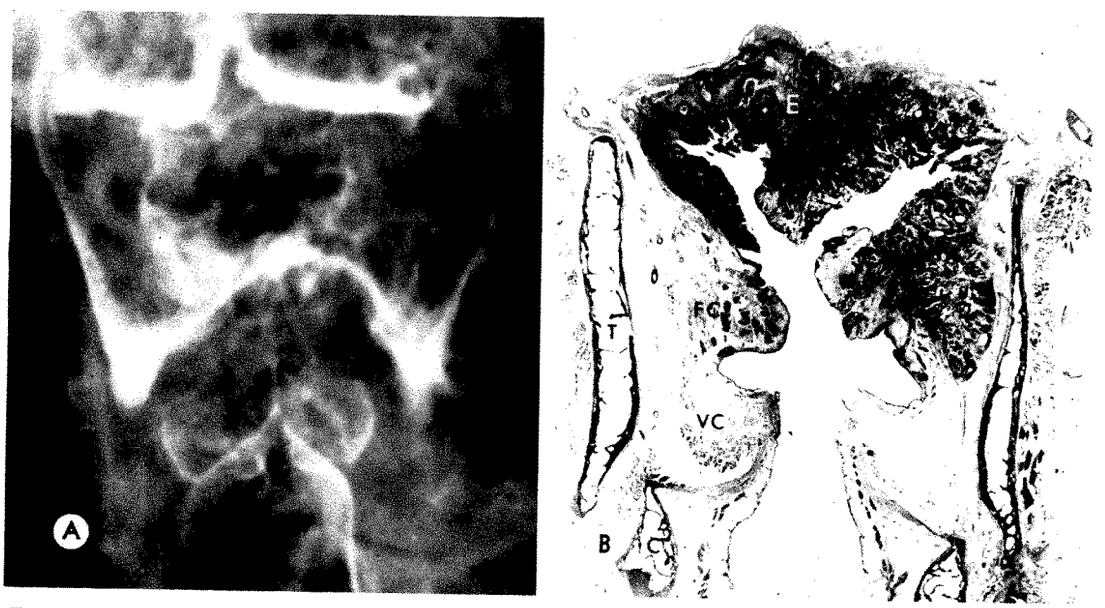


FIG. 8. Case VIII. (*A*) Laryngogram and (*B*) coronal section of a larynx taken at the level of the middle third of the vocal cords. There is a good correlation between the laryngogram and the specimen with respect to the mucosal extent of this large supraglottic carcinoma. The roentgenographic studies, however, did not assess the cartilage destruction or the deep extent of the tumor. C = cricoid; E = epiglottis; FC = false cord; T = thyroid ala; VC = vocal cord.

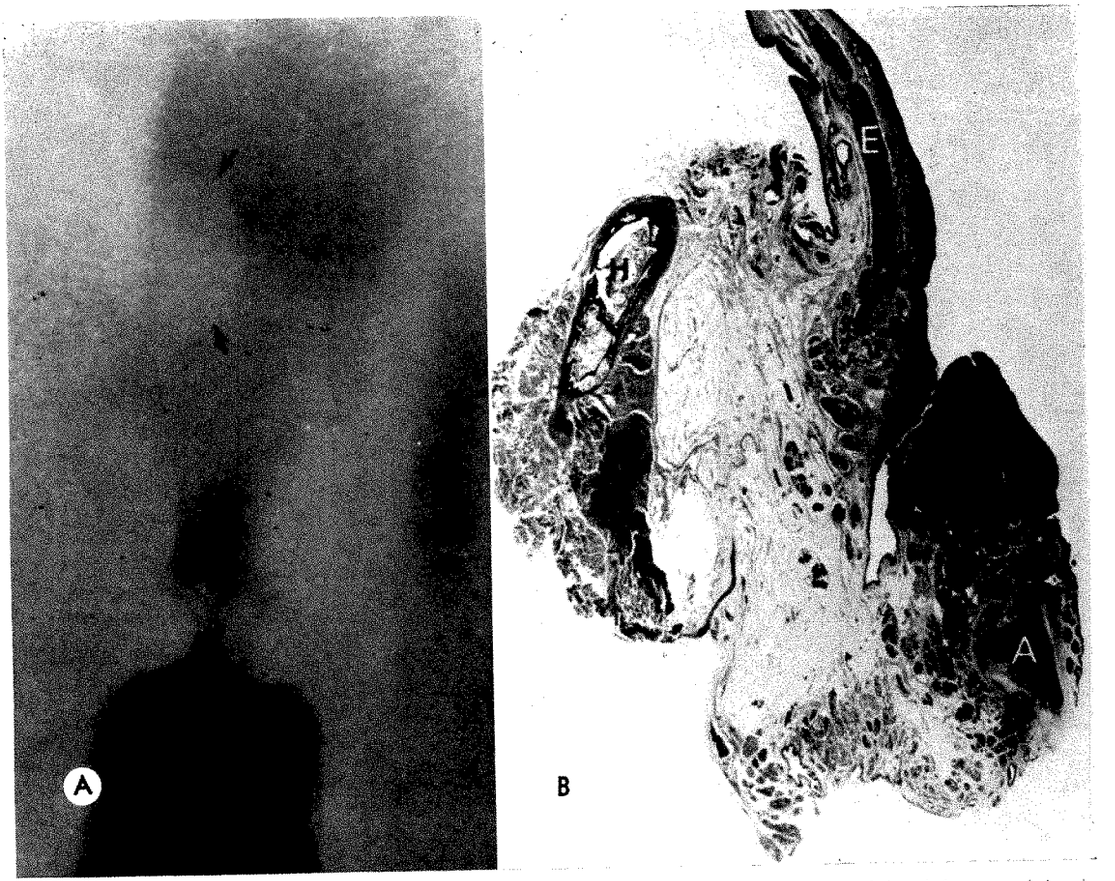


Fig. 9. Case IX. (*A*) Tomogram and (*B*) sagittal section of a larynx with a carcinoma of the right aryepiglottic fold. The surface distribution of the tumor, as illustrated by the roentgenographic studies (arrows), correlated well with the tumor in the specimen. A = arytenoid cartilage; E = epiglottis; H = hyoid bone.

of the aryepiglottic fold to involve the medial aspect of the right piriform fossa.

Comment. As the tumor had a rather superficial distribution and did not destroy deeper structures, the clinical and roentgenographic studies were extremely well correlated with the histopathologic findings.

Case X. (Fig. 10, *A* and *B*) Mr. D.O.'S., aged 51 years, smoked 20–40 cigarettes per day. He complained of recurrent hoarseness for 4 years and presented with acute airway obstruction. He was found to have a large tumor involving both vocal cords, false cords and the anterior commissure and received 5,500 rads of Co^{60} teletherapy. Following the radiation therapy he continued to have airway obstruction and a direct examination was performed 4 months later.

Laryngoscopy. Hypertrophic edematous firm tissue in the subglottic region but with no definite tumor identified.

Tomography. Circumferential obstruction of the airway involving the glottic and subglottic region.

Treatment. Total laryngectomy.

Pathology. Virtually complete obstruction of the airway subglottically by a large mass of fibrous connective tissue and granulation tissue. No residual tumor identified. Extensive necrosis and destruction of the cricoid cartilage with abscess formation. Fragments of keratin and foreign body giant cells were scattered through the fibrous connective tissue and granulation tissue, but no viable tumor could be identified.

Comment. The differential diagnosis of recurrent or residual tumor from extensive fibrosis and granulation tissue is extremely difficult, both clinically and roentgenographically. In this particular case there was no residual viable tumor identified. Despite the extensive destruction of the laryngeal cartilages, accurate assessment of this destruction by

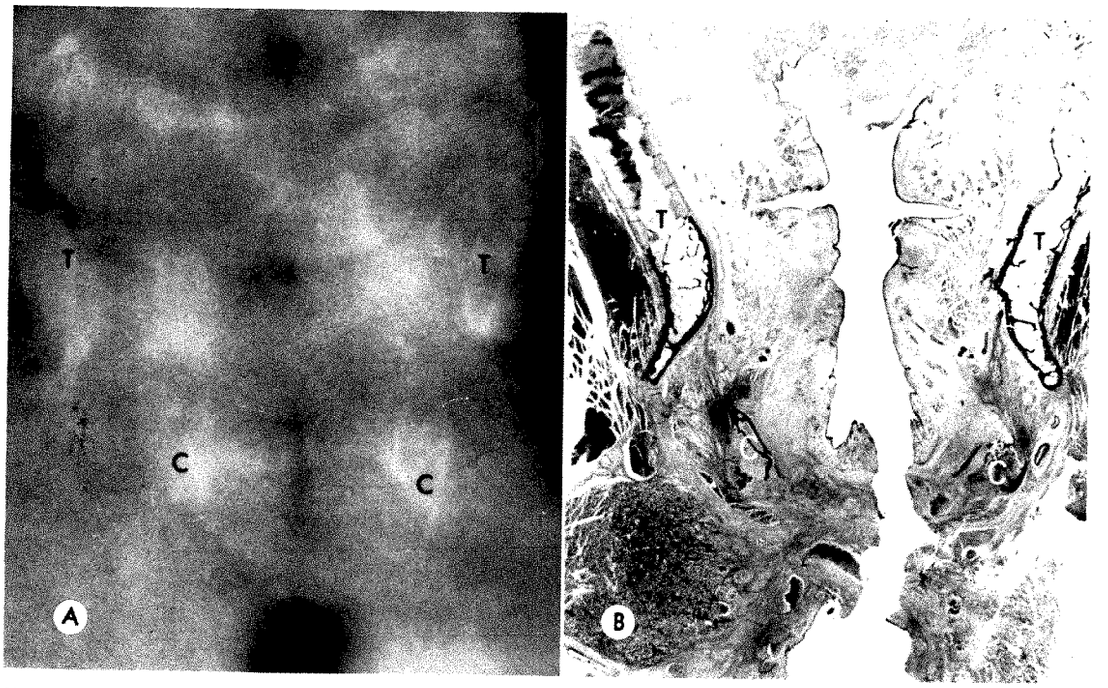


FIG. 10. Case X. (*A*) Tomogram and (*B*) coronal section of a larynx taken at the level of the posterior third of the vocal cords. There is no residual carcinoma in this specimen (post irradiation). The marked subglottic stenosis of the airway due to extensive fibrosis and abscess formation could not be distinguished roentgenologically from residual tumor, nor could the gross destruction of the cricoid cartilage be roentgenologically assessed. C = cricoid cartilage; T = thyroid ala.

tomographic means was extremely difficult due to the irregular ossification of the cartilaginous structures. There was no sign of previous tumor in the false cord region which emphasized the clinical difficulties in assessing the tumor growth in the vertical plane.

DISCUSSION

The larynx is one of those organs of the human body that can be directly inspected and it would seem logical that tumors arising in this organ should be easy to evaluate and classify. This is, however, not true—the external examination with palpation will give information regarding fixation to surrounding structures. Indirect laryngoscopy (mirror) and direct laryngoscopy usually give accurate information regarding tumor extension in the *horizontal* plane. The craniocaudal extension is much more difficult to evaluate, especially in patients with large tumors. Accurate assessment of the vocal cord mobility is usually easily obtained with these procedures as well. Additional information can be gained by roentgenologic examination. Soft tissue roentgenograms, tomograms, and laryngograms may compensate for the clinical difficulties, especially in assessing the *vertical* extent of such tumors. Even more sophisticated methods, such as cineroentgenography can provide additional information.

We have compared whole organ sections of larynges with the preoperative tomograms and laryngograms. In many of our cases there is an excellent correlation between the mucosal extent of the tumor and the clinical and roentgenologic assessments. Tomograms and laryngograms permit accurate assessment of the majority of tumors, but small tumors may be completely missed (Case VII). In our center the tomo-

grams are taken at 5 mm. levels and tumors smaller than 5 mm. in diameter may not be visualized. Circumferential and symmetric tumor growths can be easily overlooked (Case III), as much of the roentgenologic evaluation is based on asymmetry between the 2 sides. The greatest problem, however, is left unsolved—both the clinical and roentgenologic examinations fail to accurately evaluate the deep invasion of the tumor. The irregular ossification of the laryngeal cartilages makes assessment of cartilage destruction and spread outside the laryngeal framework difficult. Better methods of assessment are necessary in order to more accurately evaluate laryngeal carcinomas. This is of particular importance in conservation surgery, where the surgical technique necessitates very accurate assessment of the extent of tumor growth.

In many centers full use is not being made of presently available diagnostic techniques. To make full use of the present somewhat inadequate methods of assessment there must be a very close liaison between the laryngologist, the diagnostic radiologist, and the surgical pathologist. The diagnostic radiologist must be fully aware of the problems and questions which must be answered about each specific case prior to the commencement of therapy.

SUMMARY

Roentgenologic examination of the larynx is of invaluable help in the assessment and classification of laryngeal tumors. Soft tissue roentgenograms, tomograms and laryngograms are complementary to each other and add to the clinical examination.

We have compared whole organ serially-sectioned laryngeal carcinoma specimens with preoperative tomograms and laryngograms in a large number of clinical cases and have chosen illustrative material from 10 such cases.

Tomograms and laryngograms provide accurate assessment and evaluation of the surface extension of such tumors.

The assessment of deep invasion with cartilaginous destruction and spread outside the laryngeal framework, however, is extremely difficult, both clinically and by the currently used roentgenologic techniques.

Small tumor lesions, and extensive postoperative edema are difficult to evaluate roentgenologically.

A plea is made for closer liaison between the diagnostic radiologist, the laryngologist and the surgical pathologist.

The need for better methods of assessing deep extension of tumor growth is stressed.

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GLOTTIC CANCER*

AN ANALYSIS OF RECURRENCE AS RELATED TO DOSE, TIME, AND FRACTIONATION

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IT IS almost universally accepted that radiotherapeutic management of early glottic cancers can result in excellent survival rates;[14] and, if follow-up is conscientious on the part of patient and doctor, early recurrence can be detected and salvage obtained by laryngectomy or partial laryngectomy[1] in selected cases.

Our experience with glottic cancer in terms of survival (Table I) and surgical salvage of radiation failures (Table II) is little different from that of others,[1,14] but a sequential analysis of radiation recurrences in relation to dose, time, and fractionation showed several interesting trends that will comprise the basis of this report.

MATERIAL AND METHOD

This study was a retrospective analysis of 134 cases of early glottic cancer treated at the University of Chicago between 1937 and 1970. Ninety-three of the cases were treated primarily by irradiation and 41 were treated primarily by surgery. The majority of the surgically managed cases occurred before 1953 and the onset of the supervoltage era in radiotherapy. A subgroup of 69 cases treated between 1955 and 1970 with supervoltage radiations (Table III) was used to generate the data for the sequential analysis of recurrence rates. Cases treated with orthovoltage roentgen rays before 1955 were eliminated because we felt it desirable to eliminate the factor of RBE (Relative Biologic Effect) in the analysis. The cases were staged according to the criteria of the American Joint Committee 1962[7] (Table IV) by reviewing the findings of direct laryngoscopy, indirect laryngoscopy, tomography, and laryngography. We considered the findings of direct laryngoscopy to be more reliable than those of indirect laryngoscopy and used these findings primarily to stage patients. Only glottic cancers Stages $T_0N_0M_0$, $T_1N_0M_0$, $T_2N_0M_0$, and $T_3N_0M_0$ were analyzed for this report. For the $T_3N_0M_0$ cases only those glottic tumors with subglottic extension were included, while those with probable extension to the ventricle were excluded. The latter were excluded because of the difficulty of determining their true extent and the general lack of good laryngography. The true cord lesions with subglottic extension were more easily defined on the basis of tomograms and a few good laryngograms. All recurrences were biopsy proven and follow-up was in general very good due to the efforts of our Tumor Registry.

Since 1937, tumor dose has been calculated using central axis per cent depth dose. From Figure 1 it is apparent that the dose at the anterior commissure is greater than the central axis dose, and that the dose at the posterior commissure is less than the central axis dose. Compensators and wedges were not used to correct for this discrepancy in dose distribution. The fields were opposed in all instances, and were small in the majority of cases, measuring 5×5 cm. or 6×6 cm. in 67 of 93 cases. In 26 cases the fields were larger and encompassed not only the larynx but

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TABLE I

GLOTTIC CANCER: FOLLOW-UP AND SURVIVAL* AMONG 134 CASES TREATED PRIMARILY BY RADIATION (93) AND SURGERY (41)

(University of Chicago 1937–1970)

Stage	Total Cases	Lost		Died of Intercurrent Disease		Died of Cancer		NED		Cumulative Survival*	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	5 Yr.	10 Yr.
$T_0N_0M_0$	9	2	22	1	11	1	11	6	67	.68	.51
$T_1N_0M_0$	49	1	2	10	20	4	8	44	82	.87	.77
$T_2N_0M_0$	59	0	0	20	34	8	13	51	87	.84	.62
$T_3N_0M_0$	17	0	0	2	12	7	41	10	59	.43	.43
Total	134	3	2	33	25	20	15	111	83	.79	.65

* Cutler—*J. of Chronic Disease*, 1958, *8*, 699.
NED = No evidence of disease.

the regional lymph nodes as well.

All doses in rads were recorded directly from the chart and are 3 per cent greater than the actual central axis midplane dose by the formula: Dose in rads = % depth dose × back scatter factor × C_λ × D_{max}. By substitution of 1.02 back scatter factor for a 6×6 cm. field, and .95 for C_λ, a product of .97 results, meaning that all recorded doses should be multiplied by .97 to arrive at a true central axis midplane dose. This was not done because the estimated accuracy of daily setup, calibration of output and measurement of per cent depth doses were probably no better than ±3 per cent.

RESULTS

Recurrence and surgical salvage. The distribution of recurrence and surgical salvage for each stage is shown in Table II. Recurrence of 3 of 9 $T_0N_0M_0$ lesions was disturbing, since it seemed to us that the earliest lesions should have the least likelihood of recurrence. Perhaps if the truth

TABLE II

GLOTTIC CANCER: RADIATION RECURRENCES AND SURGICAL SALVAGE

(University of Chicago 1937–1970)

Stage	Irradiation Alone	Biopsied Recurrence		Surgical Salvage	
	No.	No.	Per Cent	No.	Per Cent
$T_0N_0M_0$	9	3	33	1	33
$T_1N_0M_0$	38	9	24	7	79
$T_2N_0M_0$	40	9	23	8	89
$T_3N_0M_0$	6	4	67	1	25
Total	93	25	27	17	68

TABLE III

GLOTTIC CANCER: DISTRIBUTION OF CASES TREATED BY SUPERVOLTAGE RADIATION

(University of Chicago 1955–1970)

Stage	No.
$T_0N_0M_0$	6
$T_1N_0M_0$	28
$T_2N_0M_0$	30
$T_3N_0M_0$	5
Total	69

were known, those lesions were truly invasive or there was excessive delay in treating them radically. The recurrence of 9 of 38 $T_1N_0M_0$ lesions, 9 of 40 $T_2N_0M_0$ lesions, and 4 of 6 $T_3N_0M_0$ lesions seemed reasonable. Admittedly, little value can be placed on the recurrence rates of the $T_0N_0M_0$ and $T_3N_0M_0$ lesions, because of the small numbers involved. The one $T_0N_0M_0$ case and the one $T_3N_0M_0$ case were each salvaged by laryngectomy. Surgical salvage for the $T_1N_0M_0$ cases included 1 laryngectomy, 2 laryngectomies with neck dissection, 2 partial laryngectomies and 2 laryngofissures. Surgical salvage for the $T_2N_0M_0$ cases included 6 laryngectomies, 1 laryngectomy and neck dissection, and 1 partial laryngectomy.

TABLE IV

T—STAGING FOR GLOTTIC CANCER

(American Joint Committee on Cancer Staging and End Results Reporting, 1962)

T_0—Carcinoma *in situ*

T_1—Tumor confined to one vocal cord and mobility of cord remains normal

T_2—Tumor involving both cords with normal mobility of cords, or tumor of one or both cords with fixation of cord(s)

T_3—Tumor extending from cords either to subglottic region or to supraglottic region, *i.e.* to ventricular bands or ventricles

TIME OF RECURRENCE

The number of biopsied recurrences that occurred within 2, 3, and 5 years for each stage is shown in Table V. It seemed unusual that only 5 of 9 $T_1N_0M_0$ cases and 6 of 9 $T_2N_0M_0$ cases recurred within 2 years, since we suspected that the majority of cases would recur before 2 years. It was not until 5 years that 80 per cent of cases or greater recurred. Horiot *et al.*[6] reported a similar phenomenon of late recurrences for glottic cancer, but to a lesser degree. Sixty-six per cent of their cases recurred within 2 years and 88 per cent within 3 years.

When the glottic cancers treated in the supervoltage era were analyzed separately from those treated in the orthovoltage era, fewer late recurrences were noted (Table VI), but the difference is statistically insignificant in view of the small number of cases.

SITE OF RECURRENCE IN RELATION TO PRIMARY TUMOR

Review of a total of 25 recurrences showed that 20 occurred at the same site as the primary, 2 on the opposite cord, 1 at the anterior commissure, and 2 were generalized endolaryngeal recurrences involving both cords (Table VII).

SEQUENTIAL ANALYSIS OF SUPERVOLTAGE, DOSE, NSD* AND RECURRENCE

Figure 2 depicts a sequential analysis of per cent cases treated with supervoltage, and the average dose in rads, the average NSD* and the average recurrence rates for 5 year periods from 1955 to 1970. With the installation of supervoltage equipment in 1953, there was a rapid rise in the number of cases treated by supervoltage until all cases were treated with supervoltage beyond 1960. Orthovoltage cases were not

* NSD represents the Nominal Standard Dose in rets according to the Ellis[2] formula:

$$NSD = \frac{\text{total dose}}{T^{0.11} \times N^{0.24}}$$

where T represents the treatment time in days, and N the number of fractions.

TABLE V

GLOTTIC CANCER: TIME OF RADIATION RECURRENCE
SUPERVOLTAGE+ORTHOVOLTAGE ERAS

(University of Chicago 1937–1970)

Stage	Biopsied Recurrence	Within 2 Years	Within 3 Years	Within 5 Years
$T_0N_0M_0$	3	3 (100%)	3 (100%)	3 (100%)
$T_1N_0M_0$	9	5 (56%)	5 (56%)	8 (89%)
$T_2N_0M_0$	9	6 (67%)	7 (78%)	7 (78%)
$T_3N_0M_0$	4	3 (75%)	3 (75%)	3 (75%)

TABLE VI

GLOTTIC CANCER: TIME OF RADIATION RECURRENCE
SUPERVOLTAGE ERA

(University of Chicago 1955–1970)

Stage	Biopsied Recurrence	Within 2 Years	Within 3 Years	Within 5 Years
$T_0N_0M_0$	2	2 (100%)	2 (100%)	2 (100%)
$T_1N_0M_0$	6	4 (67%)	4 (67%)	6 (100%)
$T_2N_0M_0$	6	5 (83%)	5 (83%)	5 (83%)
$T_3N_0M_0$	3	2 (67%)	2 (67%)	2 (67%)

represented graphically because there were few cases and there were no general trends. Orthovoltage doses were low and ranged from 4,800 to 5,500 rads at the midline of the larynx; NSD was also low ranging from 1,505 to 1,550 rets.

With progression into the supervoltage era (1953–1970), the dose and NSD began to rise, reaching a maximum of 6,700 rads average dose and 1,900 rets average NSD for the last 5 year period (1965–1970).

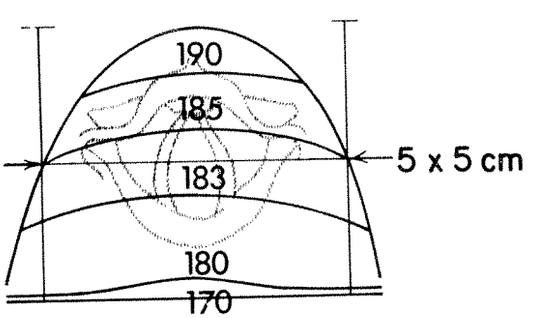


FIG. 1. Isodose pattern within larynx, using opposed ports, without compensators (2 mev. roentgen rays, 100 cm. source skin distances).

TABLE VII

GLOTTIC CANCER: SITE OF RECURRENCE IN RELATION TO PRIMARY SITE

(University of Chicago)

No. of Recurrences	Same Cord	Opposite Cord	Anterior Commissure	Both Cords
25	20	2	1	2

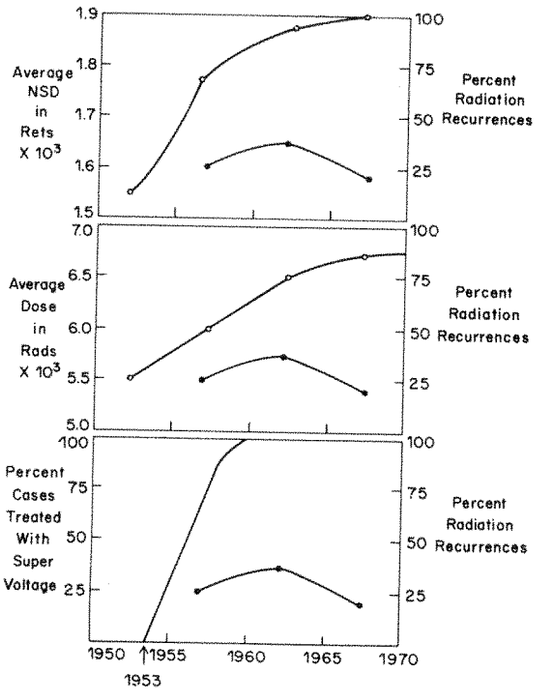


FIG. 2. Relationship of supervoltage radiation, dose, NSD, and recurrences to time in the treatment of glottic cancer (University of Chicago).

Such a rise indicates a gradual awareness on the part of the clinician that such doses could be tolerated by the larynx with supervoltage radiations. As stated previously, a subgroup of 69 cases (Table III) treated by supervoltage radiations between 1955 and 1970 were used to generate data for a sequential analysis of recurrence rates. Follow-up was 5 years and beyond for the first two 5 year periods (1955–1960), and a minimum of 3 years for the last 5 year period (1965–1970). As noted, the average dose and NSD gradually increase during the 15 year period, and the recurrence rates range from 25, to 36, to 21 per cent for each successive 5 year period (Table VIII). Despite the gradual increase in dose and NSD, it seemed that there was little change in recurrence rates to indicate that there might be a threshold dose beyond which recurrences dropped and probability of control increased.

COMPLICATIONS

From a total of 93 cases treated by irradiation alone, there was only 1 case that developed cartilage necrosis. This was a patient who had systemic lupus erythematosus and an inflamed epithelium at initiation of therapy; he developed cartilage necrosis and a laryngocutaneous fistula after 7,300 rads (2,080 rets). In general, data on voice quality and arytenoid edema were lacking.

PROBABILITY OF CONTROL VERSUS NSD

The opposite of recurrence is lack of recurrence, or probability of control, and may be represented by the formula: $P_C = 1 - P_R$, where P_C is probability of control and P_R is probability of recurrence. By graphing probability of control *versus* NSD it was hoped that a typical sigmoid response of effect *versus* NSD could be dem-

TABLE VIII

GLOTTIC CANCER: RADIATION RECURRENCES AND PROBABILITY OF RECURRENCE IN RELATION TO THREE 5 YEAR INTERVALS (1955–1969)

(Stages T_0, T_1, T_2, T_3)

Years	No. of Cases	Recurrences	Probability of Recurrence	Average Dose in Rads	Average NSD in Rets
1955–1959	20	5	.25	6,000	1,780
1960–1964	23 (22)*	8	.36	6,500	1,880
1965–1969	26 (19)†	4	.21	6,700	1,900

* One case lost to follow-up was eliminated.
† Nineteen cases followed 3 years or longer.

TABLE IX

T_1 AND T_2 GLOTTIC CANCERS PROBABILITY OF CONTROL AND RECURRENCE IN RELATION TO NSD SUPERVOLTAGE ERA

NSD Interval	No. of Cases	No. of Recurrences	PR	No. of Controls	PC
<1,700	4	1	.25	3	.75
1,700–1,799	12	3	.25	9	.75
1,800–1,899	24	5	.21	19	.79
1,900–1,999	11	2	.18	9	.82
>2,000	7	1	.14	6	.86
Total	58	12	.21	46	.79

NSD = Nominal Standard Dose; PR = Probability of Recurrence; PC = Probability of Control.

onstrated for glottic cancer. Figure 3 is a histogram of 58 T_1 and T_2 glottic cancers showing the distribution of controlled and recurrent cases in relation to various NSD intervals. Table IX shows the probability of recurrence and probability of control for each NSD interval. The probability of control ranged from .75 to .86, indicating that the NSD range of 1,700 to >2,000 was insufficient to generate a typical sigmoid curve. Most likely these data define the upper end of the curve and it is unlikely that anyone will treat at lower doses for the purpose of accumulating data for the lower part of the curve. It is likely that a probability of control of 0.8 can be achieved with approximately 1,900 rets.

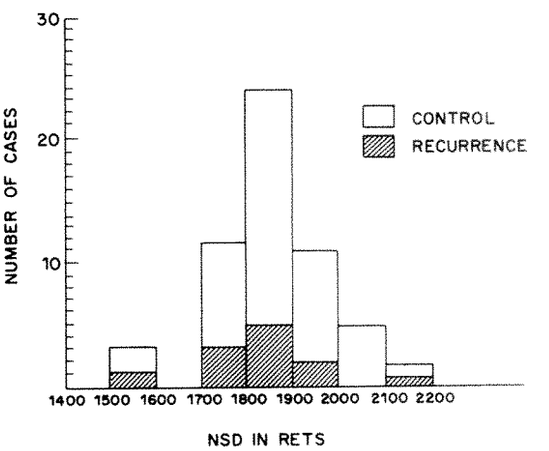


FIG. 3. T_1 and T_2 glottic cancers, radiation controls and recurrences in relation to NSD.

DISCUSSION

Glottic cancer in early stages is a good human tumor model for study of tumor control probability and recurrence rates relative to dose, time, and fractionation, because dose, time, and fractionation are the most important factors in achieving local control of the tumor. Local control of a tumor is basically determined by: (1) the physician's assessment of the extent of disease; (2) localization of the tumor in the treatment volume; and (3) a suitable dose-time-fractionation scheme. In early glottic cancer, inaccurate assessment of local extent of disease is seldom the reason for local failure, since these lesions are localized and seldom metastasize because of their small size and limited lymphatic supply. Secondly, localization of the tumor within the treatment volume is seldom significant as a cause of local failure, because of the easy accessibility of the larynx to physical examination, making precise localization possible. Thus, local failure or recurrence and tumor control probability in glottic cancer are basically a function of one parameter—the dose-time-fractionation scheme utilized.

Suit and Howard[13] in laboratory studies with small animals popularized the term "tumor cure probability" (TCP) and determined tumor control doses (TCD_{50}, TCD_{90}, etc.) for various dose-time-fractionation schemes. Mendelsohn[8] popularized the terms probability of ablation and probability of complication relative to dose, time, and fractionation and emphasized that there was an optimum scheme that would achieve maximum tumor ablation and an acceptable complication rate. These authors demonstrate that as one graphs effect of irradiated tumor or normal tissue *versus* dose, a sigmoid response occurs; *i.e.*, there seems to be a threshold dose beyond which effect, whether it be tumor ablation or normal tissue complication, increases rapidly. Of course, the radiotherapist is interested in determining this relationship between dose and effect for a wide variety of human tumors and normal tissues, but such data are difficult to determine for various reasons. One reason is that dose, time, and fractionation differ considerably for a given group of cases treated within any institution. By using the NSD concept in place of dose, one can arrive at a common denominator that is comparable despite differences in dose, time, and fractionation. It should be mentioned that NSD was originally used by Ellis[2] to determine the effects of radiation on normal tissues and may not be the correct mathematical model for human tumors. At any rate, his concept allows condensation of numerous dose-time-fractionation schemes for purposes of analysis such as the Mendelsohn type curve we attempted for T_1 and T_2 glottic cancers. As pointed out, our results over the range of NSDs listed were probably at the upper end of the sigmoid curve. Horiot *et al.*,[6] like ourselves, were unable to derive any relationship between tumor control probability and NSD because they also did not have a wide enough range of different dose-time-fractionation schemes.

One would like to know how much dose can be increased in glottic cancer without obtaining an excessive complication rate. Unfortunately, our single case of laryngeal necrosis after 7,300 rads (2,080 rets) did little to define for us the threshold NSD for laryngeal necrosis. Stewart and Jackson,[10,11] however, present data correlating dose and laryngeal necrosis that is helpful. They reported on 314 cases of early laryngeal cancer irradiated primarily, and found that laryngeal necrosis increased from zero for a low dose group (5,250 rads/3 weeks, 2,050 rets), to approximately 4 per cent for the middle dose group (5,500 rads/3 weeks, 2,140 rets), to approximately 6 per cent for the high dose group (5,750 rads/3 weeks, 2,240 rets). Their data suggest a threshold NSD of 2,050 to 2,240 rets for laryngeal necrosis and our single case (2,080 rets) is consistent with this. Doses of 7,000 rads/7 weeks (1,950 rets) are probably safely below the threshold for laryngeal necrosis. Whether other minor complications such as persistent arytenoid edema will result from such doses is uncertain. Watching for excessive complications of the latter type, we intend to give doses in the range of 7,000 rads in 7 weeks to early glottic cancer over the next 5 years to see if the probability of control can be enhanced further. It is interesting that for probability of complication, the lower portion of the sigmoid-curve is obtained and the upper end is wanting, while the reverse is true for probability of control.

Few have emphasized the importance of close long term follow-up for cases of glottic cancer treated by radiation alone. Our data and those of Horiot *et al.*[6] would indicate that recurrences occur late. It is difficult to define at what point a post radiation lesion is considered to be a recurrence and at what point it is considered a new lesion. Review of those cases that developed post radiation recurrence showed that the location of the new lesion was the same as the site of the original lesion, with the ex-

ception of 2 cases. From this we concluded that the majority of our cases were true recurrences and not new lesions.

SUMMARY

A sequential analysis of radiation recurrences of early glottic cancer in relation to a gradual increase in dose and NSD showed no significant change in recurrence rates for three 5 year periods, 1955 to 1970.

For NSD levels ranging from 1,700 to greater than 2,000 rets, the probability of control ranged from .75 to .86, indicating that the data were concentrated at the upper end of the dose response curve and that the range of NSDs was not sufficiently great to form the lower and intermediate portions of the suspected curve.

It seems likely from the data that an NSD of 1,900 rets can achieve a probability of control of approximately 0.8.

Our single complication and the data of Stewart and Jackson would indicate that the NSD threshold for laryngeal necrosis approximates 2,050 to 2,240 rets.

Long term follow-up for primarily irradiated glottic cancer is emphasized, since a number of late recurrences were noted and because excellent salvage was obtained by partial or total laryngectomy.

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RADIATION THERAPY IN EARLY CARCINOMA OF THE VOCAL CORDS*

A CHANGE IN FRACTIONATION

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EARLY squamous cell carcinoma of the vocal cords is a radiocurable disease and, in most cases, radiation therapy is the treatment of choice.[4,5,7] Surgical treatment provides virtually certain cure, but radiation therapy, properly applied, eliminates the need for surgery in most cases, while not compromising the result of surgery in the few patients who fail to respond. Aside from the major advantage of retaining his anatomic integrity and his voice, the patient encounters minimal morbidity and minimal, if any, occupational interruption associated with therapy.

Although a wide variety of radiotherapeutic techniques is employed, most centers are presently delivering 6,000 rads tumor dose in 30 fractions over a period of 6 weeks, based on the feeling that this dosage and schedule is necessary for achieving adequate local control of tumor with minimal complications.

Since a substantial number of patients at our institution continued to work during therapy and many were traveling long distances, an alternate treatment method was established, utilizing a decreased number of fractions and increased dose per fraction. Although the dose rate is somewhat different, this method of fractionation has also been employed in a prospective study sponsored by the British Institute of Radiology.[2,3]

The purpose of this study is to compare the 2 techniques of irradiation with regard to: (1) survival; (2) incidence of complications of irradiation; and (3) quality of voice.

MATERIAL

The material consists of 113 cases fulfilling the following requirements:

(1) Diagnosis of squamous cell carcinoma of the vocal cords established histologically.

(2) Lesion staged as T_1 or T_{2A}, a modification of the American Joint Committee for Cancer Staging:[6]

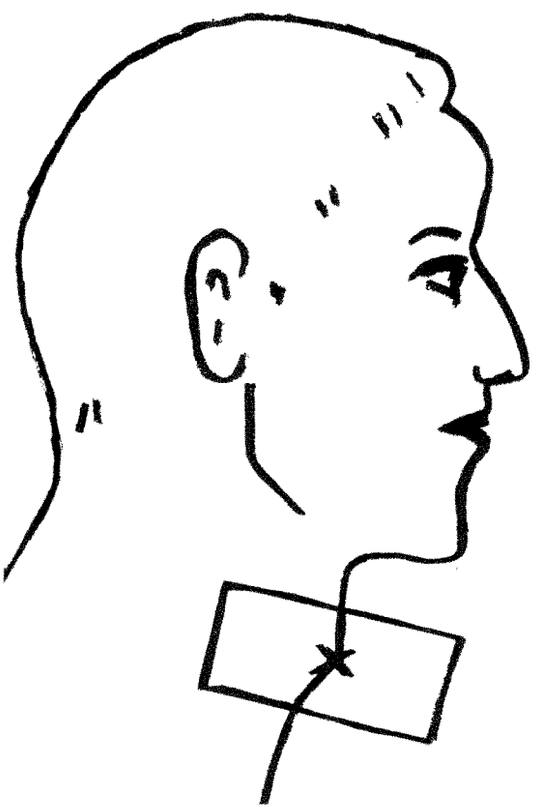


FIG. 1. Portal arrangement for early carcinoma of the vocal cord.

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TABLE I

COMPARISON OF AGE, SEX, RACE AND STAGE

Fractionation	Mean Age	Sex		Race		Stage		Total
		M	F	W	N	T_1	T_{2A}	
3×	61	61	2	58	5	50	13	63
5×	61	49	1	44	6	37	13	50

(a) "T_1" is defined as a lesion limited to one vocal cord; mobility remains normal.

(b) "T_{2A}" is defined as a lesion limited to one vocal cord and the anterior commissure, or both cords and/or the anterior commissure.

"A" indicates no limitation of motion.

(3) Full course of radiation therapy received at Duke University Medical Center.

(4) No previous treatment for cancer of the larynx.

(5) Available for follow-up at 2 years.

METHOD OF TREATMENT

The patients were all treated with Co^{60} teletherapy at the rate of approximately 1,000 rads tumor dose per week for 6 weeks. One group was treated 5 times weekly for a total of 30 fractions; the other group was treated 3 times weekly for a total of 18 fractions.

The beam was extended across the anterior skin profile in a single lateral 5×10 cm. field as shown in Figure 1. This technique avoids underdosage to the anterior commissure because of the penumbra.[1] Thus, all parts of the cords are within the high-dose area of the beam. Dose is calculated at a depth of 2.5 to 3 cm.

The patients were examined weekly during therapy, monthly for the first year after treatment and quarterly thereafter by both otolaryngologists and radiation therapists. Frequent and repeated examinations allowed for the interruption of treatment in the occasional patient whose mucosal reaction was more severe than expected or for the delivery of additional radiation to the patient whose response was less pronounced than desired.

In those cases where there was recurrence of tumor or chondronecrosis, the patient underwent the appropriate surgery, which in most cases was a total laryngectomy.

RESULTS

The group which received treatment 3 times weekly and the group which received treatment 5 times weekly were essentially comparable in all respects. Both show a

TABLE II

ABSOLUTE SURVIVAL
(2 years)

Fractionation	No.	Alive		Dead with Disease		Dead of ICD	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
3×	63	61	96.8	0	—	2	3.2
5×	50	47	94.0	1	2.0	1	2.0
Total	113	109	96.5	1	0.9	3	2.7

ICD = intercurrent disease.

TABLE III

PATIENTS REQUIRING SURGERY FOLLOWING RADIATION

Fractionation	No.	Radiation Alone		Radiation and Surgery		Reasons for Surgery
		No.	Per Cent	No.	Per Cent	
3×	63	57	90.5	6	9.5	all recurrences
5×	50	44	88.0	6	12.0	4 recurrences, 1 necrosis
Total	113	101	89.4	12	10.6	1 severe inflammation

mean age of 61 years, at least 97 per cent males, approximately 90 per cent white and similar distribution of T_1 and T_{2A} lesions (Table I).

SURVIVAL

A comparison of the over-all 2 year survival rates is shown in Table II. The figures are absolute and do not exclude patients dead of intercurrent disease. The survival rates for both methods of treatment are approximately equivalent—96.8 per cent for the 3 times weekly and 94 per cent for the 5 times weekly. A total of 109/113 (96.5 per cent) patients in this series was alive and free of disease 2 years following treatment. Three patients died of intercurrent disease and were free of tumor. The relative survival rate, which excludes those dead of intercurrent disease, was 98 per cent.

These survival rates also include radiation failures, who for purposes of this study include patients in whom there was recurrent tumor or severe complication of irradiation requiring surgery. Following a full course of irradiation, 6 patients in each group underwent laryngectomy or cordectomy (Table III). Recurrent tumor was found in 10 of 12 specimens. In 2 specimens, both in the 5 times weekly group, no tumor was found. In 1, there was chondronecrosis; in the other, marked inflammation and scarring.

Of the 12 patients who underwent surgery, tumor persisted in 2 patients, 1 in each group (Table IV).

There is no significant difference between T_1 and T_{2A} lesions with regard to survival or recurrence rate (Table V).

INCIDENCE OF COMPLICATIONS

Early. The incidence of severe early complications necessitating interruption of radiation therapy is shown in Table VI. Approximately 95 per cent of the 113 patients showed no complications. Those treated 3 times weekly had fewer complications than those treated 5 times weekly, regardless of the extent of the lesion.

Late. The incidence of complications observed 6 months or more after the begin-

TABLE IV

PERSISTENT TUMOR FOLLOWING SURGERY

Fractionation	No.	NED 2 Years Post Surgery	Persistent Disease
3×	6	5/6	1/6
5×	6	5/6	1/6

NED = No evidence of disease.

TABLE V

COMPARISON OF ABSOLUTE SURVIVAL—T_1 AND T_{2A} LESIONS

Fractionation	No.	T_1		T_{2A}	
		No.	Per Cent	No.	Per Cent
3×	63	49/50	98.0	13/13	100.0
5×	50	36/37	97.3	11/13	85.0
Total	113	85/87	97.7	24/26	92.3

TABLE VI

INCIDENCE OF EARLY COMPLICATIONS

Early Complications	3×		5×	
	T_1	T_{2A}	T_1	T_{2A}
None	50	12	34	11
Severe mucositis only		1	1	
Severe edema and mucositis			1	1
Severe skin reaction			1	
Poor general health				1
Total	50	13	37	13

ning of the radiation therapy is shown in Table VII. There was 1 patient with chondronecrosis and 2 with severe persistent inflammation; all were in the 5 times weekly group.

QUALITY OF VOICE

The degree of hoarseness was observed 1 year after the initial radiation treatments (Table VIII). A normal voice was retained in approximately 70 per cent of the patients in each group. Slight to moderate hoarseness occurred in 30 per cent.

DISCUSSION

Similar groups of patients receiving radiation therapy in 3 fractions per week and 5 fractions per week have been compared.

Survival data have been given at 2 years. It is the experience of several authors that recurrence or persistence of tumor will occur within the first 2 years and that the 2 year survival rates are a good indication

TABLE VII

INCIDENCE OF LATE COMPLICATIONS

Late Complications	3×		5×	
	T_1	T_{2A}	T_1	T_{2A}
None	50	13	34	13
Chondronecrosis			1	
Persistent inflammation			2	
Total	50	13	37	13

TABLE VIII

QUALITY OF VOICE—POST-TREATMENT

Quality of Voice	3×		5×	
	No.	Per Cent	No.	Per Cent
Normal	43	70	37	74
Slight (occasional) hoarseness	13	20	7	14
Moderate hoarseness	7	10	3	6
Severe hoarseness			3	6

of ultimate survival.[1,7] This is substantiated by this group of patients. Table IX shows that the relative survival (*i.e.*, excluding deaths due to intercurrent disease) at 2 years and 5 years is approximately the same.

It is always difficult to make valid comparisons of such subjective factors as quality of voice and complications. However, in this study, the 3 times weekly group shows both a lower incidence of radiation complications and less severe hoarseness than the 5 times weekly group. The 3 severe complications were all in the 5 times weekly group. Of course, the numbers are small and not significant. Two of these required eventual laryngectomy. Comparison of the 2 methods by use of the Ellis formula reveals that the nominal single dose (NSD) for the 3 times weekly method is 2,000 rets and for the 5 times weekly method is 1,760 rets. Despite the difference in the nominal single dose, there did not appear to be any difference in the complication rate.

TABLE IX

COMPARISON OF RELATIVE SURVIVAL AT 2 AND 5 YEARS

Fractionation	2 Years		5 Years	
	No.	Per Cent	No.	Per Cent
3×	61/62	98.4	32/33	97
5×	47/48	97.9	33/33	100
Total	108/110	98.0	65/66	99

The practical and economic advantages of decreasing the number of fractions are numerous for both patients and staff. Reduction of the number of visits by 40 per cent conserves time for all the patients and allows for minimal interruption for those patients who wish to maintain their employment status. For the staff, such a schedule represents a more efficient, economical clinical procedure and potentially allows for a greater treatment volume.

CONCLUSION

The technique presented for therapy of early carcinoma of the vocal cords is at least equivalent to the more conventional fractionation with regard to survival, incidence of complications and quality of voice.

In addition, it offers a much more convenient therapeutic approach for patient and physician.

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CARCINOMA OF THE LARYNX*

RESULTS OF RADIATION THERAPY IN 213 PATIENTS

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CARCINOMA of the laryngeal structures is well situated anatomically for successful treatment by megavoltage radiation therapy techniques, which have given excellent results especially in the treatment of small tumors involving the true vocal cords. Larger tumors of the vocal cords and those of the supraglottic larynx, however, are more difficult to control with either radiation therapy alone or with combined surgery and irradiation.

This report analyzes the results of treatment of 213 patients with carcinoma of the glottic, subglottic and supraglottic regions and supplements the prior review of patients treated at Stanford which was published in 1965.[2]

MATERIAL AND METHOD

The records of all patients with laryngeal carcinomas treated in the Stanford Division of Radiation Therapy between 1957 and 1970 were reviewed. Seventeen patients were excluded from this analysis: 10 patients with glottic lesions treated for palliation either after postlaryngectomy failure (6 patients) or for other reasons (4 patients) and 7 who were seen in consultation only. All patients were staged by the TNM system according to the UICC classification. The initial staging was used for this study except in a very few instances where an error had been made.

Sixty-seven patients with supraglottic carcinomas involving the laryngeal surface of the epiglottis, false cords, aryepiglottic folds and arytenoids were included (Fig. 1).

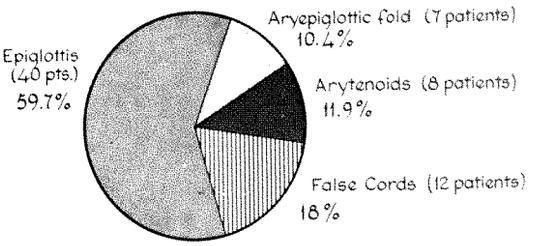


FIG. 1. Primary tumor sites, supraglottic carcinomas (67 patients).

Case accession for this group ended in late 1968, when a randomized protocol which included both advanced supraglottic and hypopharyngeal carcinomas treated by radiation therapy and/or surgery was initiated. A total of 146 patients with glottic or subglottic carcinomas treated between 1957 and 1970 were also evaluated (Fig. 2).

All of these patients were treated in the sitting position with the Stanford 4.8 mev. medical linear accelerator, using a bite block for immobilization whenever possible, as previously described.[2] Opposed 4×4 cm. or

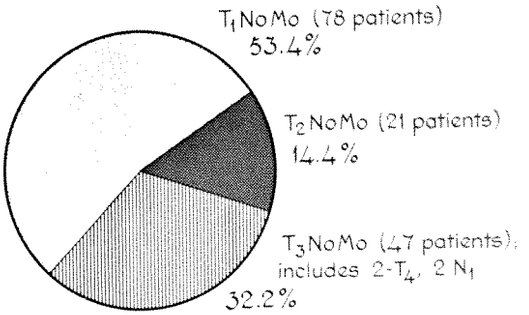


FIG. 2. TNM Stages, glottic carcinomas (146 patients).

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TABLE I

AGE AND SEX DISTRIBUTION (213 PATIENTS)

	10–19	30–39	40–49	50–59	60–69	70–79	80–89	(Total)
SUPRAGLOTTIC LARYNX (67)								
Male	1	1	10	18	25	3	0	(58)
Female				7	1		1	(9)
	20–29	**30–39**	**40–49**	**50–59**	**60–69**	**70–79**	**80–89**	**(Total)**
GLOTTIC LARYNX (146)								
Male	1	1	16	39	45	26	6	(134)
Female			7	3		2		(12)

4×5 cm. lateral wedged treatment fields were used for carcinomas of true vocal cords alone, with daily fluoroscopic pretherapy beam alignment, whereas larger opposed lateral fields combined in many instances with supplemental anterior neck treatments were used for those with supraglottic and T_3 glottic cancers. The tumor doses varied between 5,000 rads in 5 weeks and 7,000 rads in 7 weeks, but most patients treated with curative intent received a total dose of 6,600 rads in 39 to 45 days, with treatments 4 or 5 times per week. Less than 5 per cent of the patients were lost to follow-up. All patients were followed when possible in the conjoint Radiation Therapy-Otolaryngology Clinic at the Stanford University Hospital and in the ENT Clinic of the Palo Alto Veterans Administration Hospital.

The Nominal Standard Dose (NSD) for each of the 213 patients was calculated according to the methods of Ellis,[3,4,10] using the formulas

$$NSD = \frac{D}{N^{0.24}T^{0.11}}$$

and

$$N = \left(\frac{NSD}{d}\right)^{1.57}K^{0.17}$$

with treatment splits corrected for by the equation:

P (corrected partial tolerance)

$$= P\left(\frac{T_1}{T_1 + T_0}\right)^{0.11}$$

RESULTS

1. AGE AND SEX

One hundred ninety-two of the 213 patients were males (90 per cent) (Table 1). The majority were in the 6th and 7th decades of life with mean ages of 60.5 years and 57.6 years for those with glottic and supraglottic tumors, respectively. However, 32 of the patients with glottic lesions were elderly with ages of 70 to 89 years.

2. PRESENTING SYMPTOMS

As shown by Figure 3, 92 per cent or 135 of the patients with glottic lesions presented with hoarseness and 67 per cent of this group had either a normal or improved voice after radiation therapy. Considering $T_1N_0M_0$ true vocal cord lesions separately, 83 per cent of the patients in that group who were initially hoarse noted an improved voice after irradiation. A smaller percentage of the patients with supraglottic carcinomas were hoarse initially, and relatively fewer of these had a normal or improved speaking voice after radiotherapy (Fig. 4).

3. OTHER MALIGNANCIES, EXCLUDING SKIN CANCER

Second (and even third) primary tumors occurred in 34 of these 213 patients (16 per cent), the most common sites being other head and neck areas, the lungs, esophagus and kidneys (Table II).

4. METASTASES

Twenty-one of the 213 patients (10 per

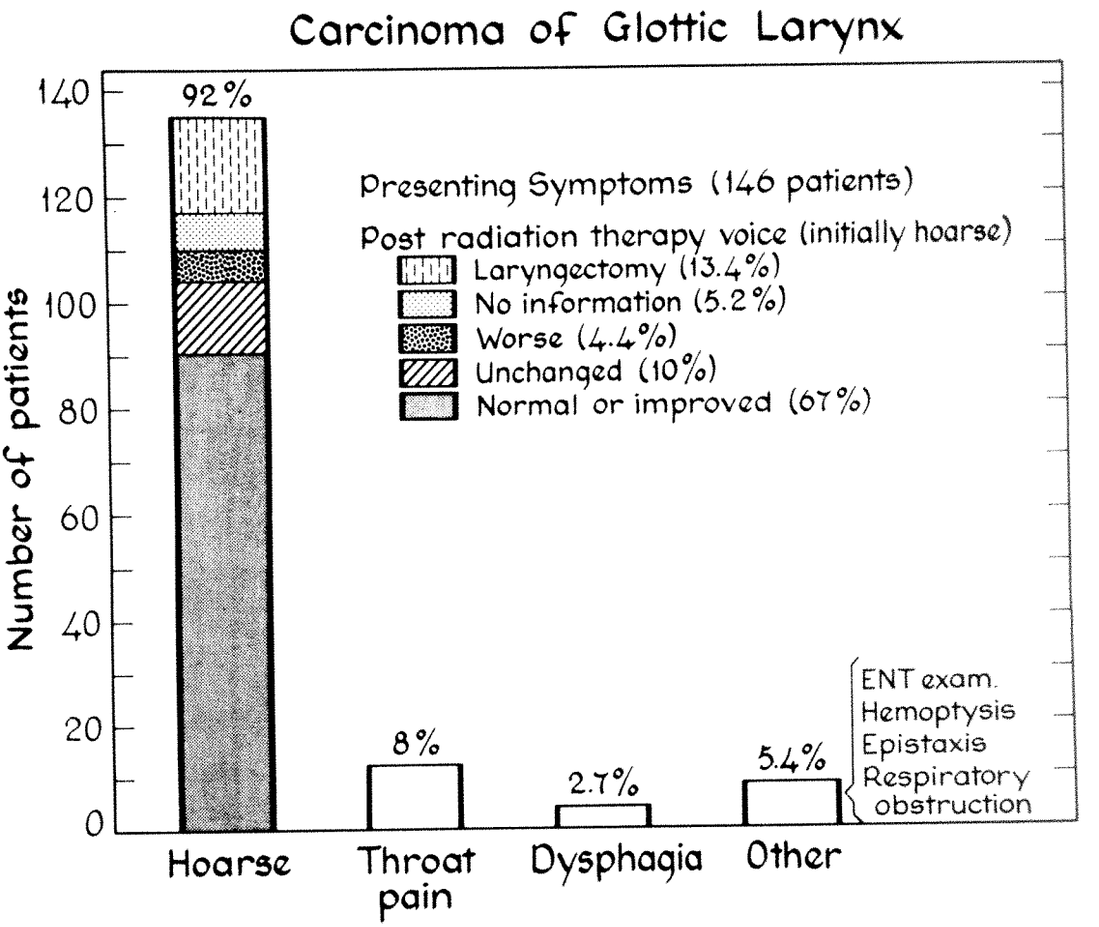


FIG. 3. Patients with glottic carcinomas: presenting symptoms and postirradiation voice in those who where initially hoarse.

cent) eventually developed metastatic disease with the lungs being most frequently involved. The sites of metastases are tabulated in Table III.

5. HISTOLOGY

All but 1 of the patients had biopsy proof of squamous cell carcinomas in various degrees of differentiation. There were 8 carcinomas *in situ* among those with true vocal cord tumors, but this diagnosis may have represented a minimal assessment of involvement due to sampling errors at the time of direct laryngoscopy and biopsy, as exemplified by 1 patient with presumed carcinoma *in situ*, who died with widely metastatic tumor and locally uncontrolled disease. The single patient with a biopsy diagnosis other than squamous cell carcinoma (interpreted as either oat cell carcinoma or lymphoepithelioma) also died with widespread metastatic disease and extensive local tumor.

6. INTERCURRENT DEATHS

There were numerous causes of intercurrent deaths, but these were most often due to either cardiovascular diseases or second malignancies.

SURVIVAL

1. GLOTTIC CARCINOMA

Actuarial survival by the Berkson-Gage method for the 146 patients with glottic carcinoma is shown in Figure 5, which includes intercurrent deaths as well as deaths

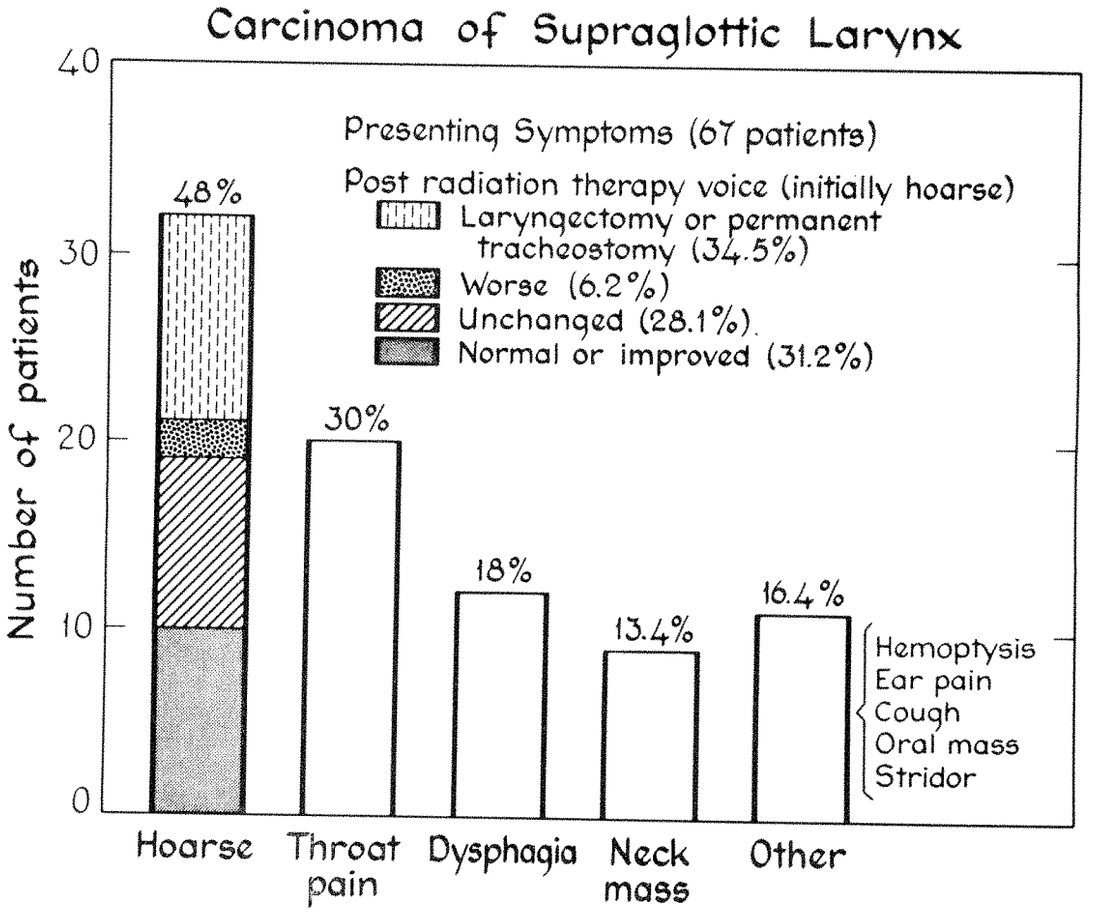


Fig. 4. Initial symptoms and postirradiation voice, patients with supraglottic tumors.

due to tumor in each group, along with the patients both withdrawn alive and lost to follow-up during each interval.

Five year survivals of 90, 80 and 59 per cent were obtained for patients with T_1, T_2 and T_3 vocal cord lesions, respectively. Table IV, an analysis of results by stage in patients with glottic carcinomas, shows that only 1 tumor related death occurred among the 99 patients with T_1 and T_2 true vocal cord lesions. Not one of these patients had cervical lymph node involvement.

In those patients with $T_1N_0M_0$ true vocal cord lesions who failed after radiation therapy, 3 of the 5 recurrences involved only the subglottic region while the fourth extended onto supraglottic structures. The fifth patient had the only true cord recurrence, suggesting that the majority of those patients with postirradiation failures in the T_1 group were initially understaged. All 4 postirradiation recurrences in those with $T_2N_0M_0$ lesions were controlled by laryngectomy. Therefore, 8 of the 9 patients with Stage T_1 or T_2 vocal cord carcinomas who had a local recurrence were salvaged by laryngectomy. Six of these patients are alive without evidence of disease and 2 have died from intercurrent causes.

In the 47 patients with Stage T_3 glottic carcinomas (including 2 patients with T_4 disease and 2 with N_1 cervical lymphadenopathy), irradiation failed to control the primary tumor in 18 patients (37.5 per cent). Six of these 18 patients had unresectable carcinoma either due to the pres-

TABLE II

OTHER PRIMARY TUMORS, EXCLUDING SKIN CANCER

SUPRAGLOTTIC LARYNX—16 OF 67 (24%)

Epiglottis (11 of 40)		Aryepiglottic, Arytenoid, False Cords (5 of 27)	
Tonsil	3	Floor of mouth, Alveolar ridge	1
Lung	3	Esophagus	1
Esophagus	3	Soft palate, tonsil	1
Tongue	2	Floor of mouth, Base of tongue	1
Lip	1	Lung	1
Pancreas	1		
Colon	1		
Melanoma	1		
(4 patients with 3 primaries)			

GLOTTIC LARYNX—18 OF 146 (12%)

T_1 (10 of 78)		T_2 (1 of 21)	T_3 (7 of 47)	
Kidney	3	Hepatoma and buccal mucosa	Hepatoma and soft palate	1
Prostate	2		Carcinoma bile duct	1
Pancreas	1		Floor of mouth	1
Floor of mouth	1		Lung	1
Mycosis fungoides	1		Pancreas	1
Uvula	1		Alveolar ridge	1
Left arytenoid (9 years later)	1		Mediastinal anaplastic carcinoma	1

ence of metastases or because of advanced local tumors. Local control, however, was obtained in 11 of 14 patients, including 2 patients who underwent planned total laryngectomy and radical neck dissection after a preoperative radiation therapy dose of 5,000 rads in 5 weeks. Six of the patients remain alive without evidence of disease following surgery, and 4 have died with local control, 1 with metastatic tumor and the others with intercurrent disease. Seven patients also underwent neck dissection at the time of laryngectomy. Two of the 7 specimens contained positive lymph nodes and 1 of these patients failed locally. All of the 5 patients with negative neck specimens remained free of disease in the operated and previously irradiated neck.

A subgroup of 32 patients with subglottic extension of carcinoma (there were no patients with identifiable subglottic disease alone without true vocal cord involvement) had an actuarial 5 year survival rate of 60 per cent, which did not differ from that of the entire T_3 group of 47 patients. Seven are alive and free of disease after radiation therapy alone and 10 have died with local tumor control, either from intercurrent disease (8 patients) or with metastatic tumor (2 patients). Five patients had un-

TABLE III

SITES OF DISTANT METASTASES

SUPRAGLOTTIC LARYNX (12 OF 67)		
	Lung	8
	Mediastinum	2
	Liver	2
	Celiac Lymph Nodes	2
	Brain	2
	Bone	2
	Gastrointestinal Tract	1
GLOTTIC LARYNX (9 OF 146)		
T_1 (1 of 78)	Cervical lymph nodes, Mediastinum, Lung, Liver, Kidneys, Bone	
T_2 (0 of 21)		
T_3 (8 of 47)	Lung	6
	Eye, Mediastinum, Skin	1
	Widespread	1

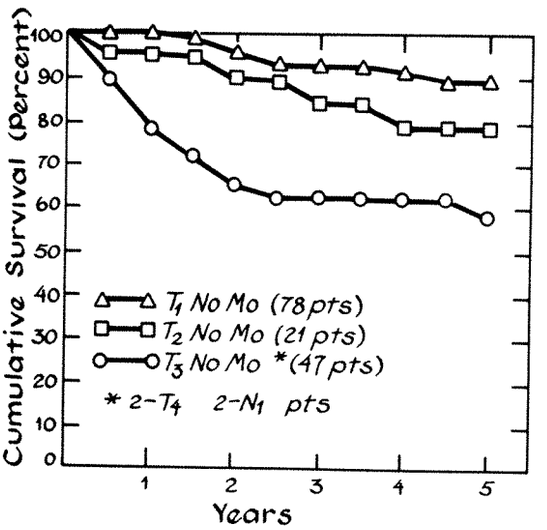


FIG. 5. Berkson-Gage actuarial survival for the 146 patients with glottic carcinomas.

resectable lesions. Local control was established in 6 of the 10 patients who underwent laryngectomy; however, 3 others were uncontrolled following surgery. The remaining patient was lost to follow-up, but was free of disease when last seen 6 months after laryngectomy. Four of these 10 patients remain alive and free of disease post-laryngectomy and 2 have died from intercurrent disease, for a total salvage of 11 patients alive without evidence of disease and 12 who died with local tumor control out of a total of 32 patients with subglottic carcinomas.

Seventeen of the 47 T_3 patients had transglottic tumors, and initial local control with radiotherapy alone was obtained in 8. Five of the 9 failures were resectable and local control was obtained in all 5. Four of these remain alive and free of disease. In the subgroup of 8 patients with both transglottic tumors and a fixed vocal cord, 7 were treated with irradiation alone with curative intent and local control was obtained in 3. A single patient who received planned preoperative radiotherapy is alive and free of disease, but only 1 of the 4 radiation failures was operable and that patient remains alive without evidence of tumor recurrence following laryngectomy.

TABLE IV

RESULTS OF TREATMENT
GLOTTIC CARCINOMA

Stage	Radiation Therapy Only				Irradiation Followed by Laryngectomy		
$T_1N_0M_0$ (78)	Alive (NED)	58	73	→	Alive (NED)	2	5
	Died (local control)	15			Died (local control)	2	
	Intercurrent	15			Died (uncontrolled)	1	
	Metastases	0					
	Died (uncontrolled)	0					
$T_2N_0M_0$ (21)	Alive (NED)	13	17	→	Alive (NED)	4	4
	Died (local control)	4			Died (local control)	0	
	Intercurrent	4			Died (uncontrolled)	0	
	Metastases	0					
	Died (uncontrolled)	0					
$T_3N_0M_0$ (47)	Alive (NED)	12	33	→	Alive (NED)	6	14
	Died (local control)	15			Died (local control)	4	
	Intercurrent)	12			Intercurrent	3	
	Metastases	3			Metastases	1	
	Died (uncontrolled)	6			Died (uncontrolled)	3	
					Lost to follow-up	1	

NED = no evidence of disease.

2. SUPRAGLOTTIC CARCINOMA

Actuarial survival for this group of 67 patients at 5 years was 41 per cent for those with epiglottic primaries and 45.5 per cent for patients with lesions of the other supraglottic sites (arytenoids, false cords and aryepiglottic folds) (Fig. 6). Fourteen of the 67 patients had T_1 lesions, 24 T_2, 8 T_3 and 21 had T_4 lesions. Table V shows the disease free (NED) survival for this group after a minimum follow-up period of 2 years. Seven of the 9 patients with large tumors and no clinically positive cervical lymph nodes (Stages $T_3N_0M_0$ and $T_4N_0M_0$) were controlled and remain free of disease, 6 of these received irradiation alone, while 3 were treated with both radiotherapy and surgery. However, patients with similar T stages, but having clinically positive cervical lymph nodes, had a much poorer survival, with only 5 of 20 being free of disease ($p < 0.05$ but > 0.02).

Fifty-two of the 67 patients were treated initially by radiation therapy with curative intent and 4 others received planned preoperative irradiation. In addition, 11 patients initially underwent surgery with curative intent, either epiglottectomy, neck dissection alone or laryngectomy prior to receiving radiation therapy for postoperative local failure (Table VI).

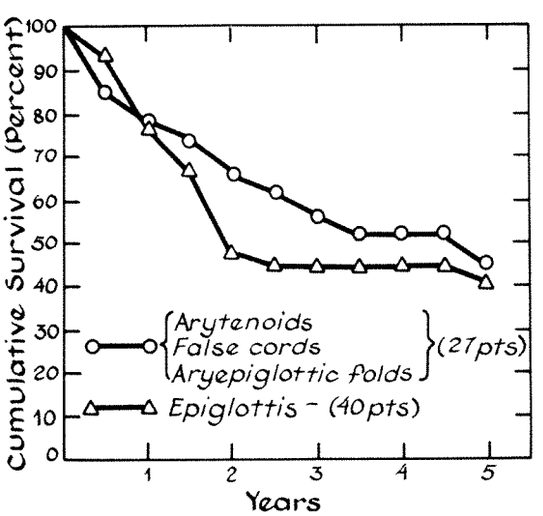


FIG. 6. Berkson-Gage actuarial survival for the 67 patients with supraglottic cancers.

TABLE V

NED SURVIVAL*
SUPRAGLOTTIC CARCINOMA

	N_0	N_1	N_2	N_3	
T_1	5/10	1/3	0/0	0/1	6/14
T_2	5/12	3/6	0/2	0/4	8/24
T_3	4/4	2/4	0/0	0/0	6/8
T_4	3/5	0/8	1/1	2/7	6/21
	17/31	6/21	1/3	2/12	

NED = No evidence of disease.
* Minimum 2 year follow-up.

Radiation therapy with curative intent resulted in local tumor control in 24 of 52 patients (46 per cent). Thirteen patients in this group died with uncontrolled local disease and had unresectable carcinoma due to either metastatic disease (8 patients) or advanced local tumor (5 patients). Surgical resection was performed after radiation therapy in 19 patients, including laryngectomy in 16 (9 of these patients also had neck dissections) and neck dissection alone in 3 others who had only recurrent cervical lymph node disease. The group of 4 patients with planned laryn-

TABLE VI

RESULTS OF RADIATION THERAPY AFTER INITIAL SURGICAL FAILURE
SUPRAGLOTTIC LARYNX

Surgery, Then Radiotherapy (11 Patients)			
Laryngectomy (4 with neck dissection)			6
Neck dissection only			3
Epiglottectomy and neck dissection			2
Alive (NED)			2
Died (local control)			
Intercurrent	0		
Metastases	3		3
Died (uncontrolled)			6

NED = no evidence of disease.

TABLE VII

COMPLICATIONS OF RADIATION THERAPY—19 OF 213 PATIENTS (9%)

Stage	Complication	No. of Patients	Nominal Standard Dose (NSD)—Rets
	SUPRAGLOTTIC LARYNX (8 OF 67 PATIENTS)		
$T_1N_0M_0$	Persistent arytenoid edema	1	2,111
$T_2N_0M_0$	Permanent tracheostomy, fixation and necrosis of epiglottis	1	2,137
$T_4N_0M_0$	Permanent tracheostomy, severe glottic edema	2	1,921, 2,052
	Edema, chondritis, epiglottic necrosis	1	2,260
T_4N_2	Myositis, irradiated cervical area	1	2,097
T_4N_3	Severe cervical induration, vocal cord paralysis	1	1,857
	Severe cervical induration, cricopharyngeal fibrosis, inanition with resultant death	1	2,006
	GLOTTIC LARYNX (11 OF 146 PATIENTS)		
$T_1N_0M_0$	Arytenoid and false cord edema	2	1,814, 1,943
	Permanent tracheostomy, laryngeal chondritis and necrosis	1	2,102
$T_2N_0M_0$	Permanent tracheostomy for chondritis and laryngeal necrosis	1	2,435
	Tracheostomy for edema at 6 months, tumor recurrence 5 months later	1	1,943
	Laryngeal chondritis, necrosis, vocal cord fixation	1	2,253
$T_3N_0M_0$	Severe arytenoid edema, including temporary tracheostomy in one patient	5	1,740, 1,822, 1,833, 1,836, 1,935

gectomies received a preoperative radiation therapy dose of 5,000–5,500 rads in 5 to 6 weeks through opposed large, lateral fields —a dose that apparently did not result in either more difficult surgery or increased postoperative complications. All 4 of these patients are alive without evidence of disease after a minimum follow-up period of 2 years and had initial TNM stages of $T_1N_0M_0$, $T_1N_1M_0$, and $T_3N_0M_0$, and $T_4N_3M_0$. Local control was also obtained in 12 of the 15 patients with resectable lesions who failed after radiation therapy and were then treated by surgery. Five of these patients are alive and free of disease, while 7 died with local tumor control, 4 from intercurrent disease and 3 with widespread metastases. Local control, therefore, was obtained in 84 per cent or 16 of the 19 patients with resectable lesions following radiation therapy, which includes the 4 patients receiving planned preoperative irradiation (Fig. 7).

Opposed lateral laryngeal fields and supplemental anterior supraclavicular ports were utilized to treat the entire neck regions of the 67 patients with supraglottic carcinomas (134 hemi-necks). One hundred twenty-three hemi-necks were available for analysis, distributed into 2 groups, those with and without clinically positive lymph nodes. Eleven hemi-necks, also irradiated, were excluded, 8 in the 4 patients who received planned preoperative radiotherapy and 3 others in patients who initially underwent neck dissections for cervical lymphadenopathy without a known primary site.

Irradiation of clinically positive lymph nodes in 53 hemi-necks resulted in local control in 32 (60 per cent), while 6 of the 21 failures were operated upon and 5 of these were salvaged by surgery. Fifteen patients could not be retreated either by radiation therapy or surgery. The lymph node control rate in the group that was treated by laryngeal irradiation ports only was 52 per

cent (13 of 25 hemi-necks controlled), whereas the control rate in those patients who had an additional low anterior neck field was 68 per cent (19 of 28 hemi-necks). Although not significant at the 0.05 confidence level, these data suggest that the supplemental low cervical-supraclavicular irradiation ports may increase the local control rate in patients with clinically positive cervical lymph nodes. However, a larger population would be necessary to test the validity of this hypothesis.

In patients with clinically negative necks, the primary laryngeal ports plus an added anterior supraclavicular field resulted in 86 per cent local control (19 of 22 necks), while 81 per cent local control (39 of 48 hemi-necks) was obtained by the use of opposed lateral laryngeal fields alone. There was no significant difference in recurrence rates between these 2 groups. Six of the 12 cervical failures in those patients with originally negative necks were resectable and local control was established in 2 of these patients. Therefore, local control was achieved in 7 hemi-necks out of a total of 12 neck dissections that were performed in all groups.

COMPLICATIONS

Postirradiation complications occurred in 19 of the 213 patients (9 per cent) and necessitated permanent tracheostomies in 5 patients and temporary tracheostomies in 2 others. Table VII lists all postirradiation complications by stage and Nominal Stan-

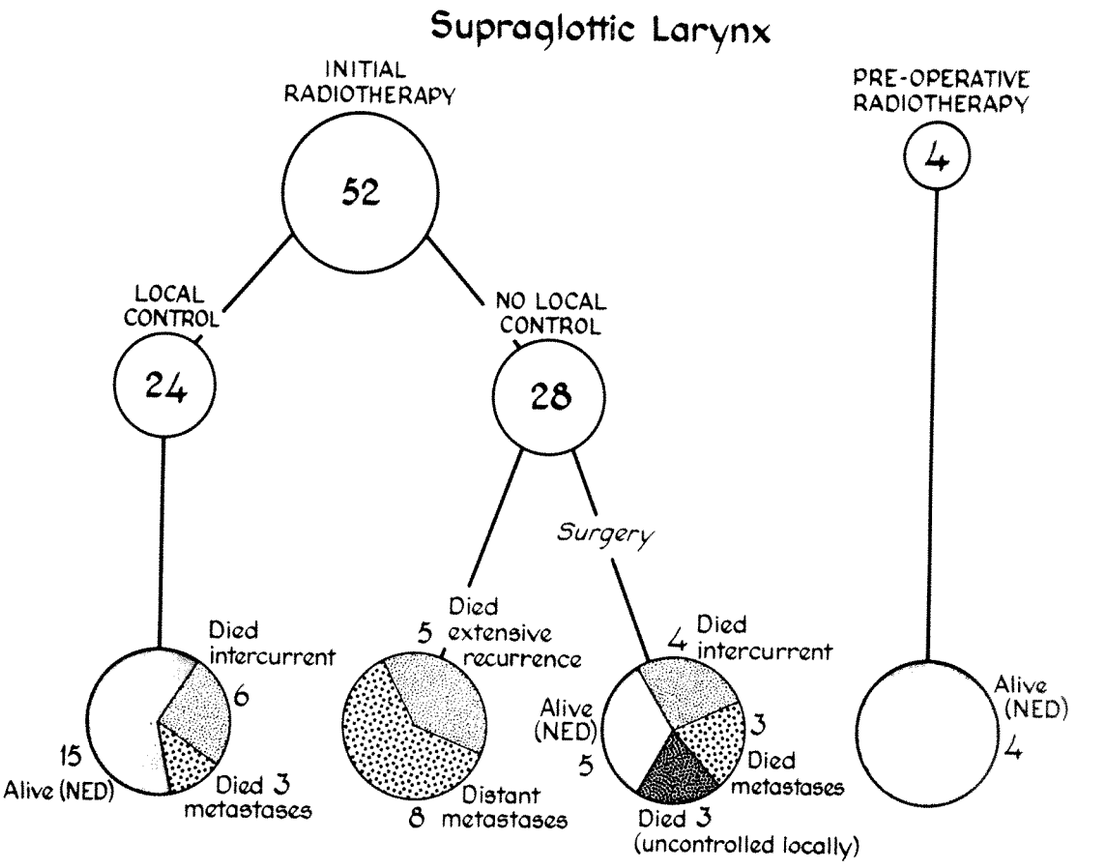


FIG. 7. Results in 56 patients with supraglottic carcinomas subjected initially to radiation therapy. Local control was established in 16 of 19 patients with resectable carcinoma, including all 4 with planned preoperative irradiation.

dard Dose (NSD). The only tumor recurrence in this group of 19 patients occurred 5 months after a temporary tracheostomy had been performed for laryngeal edema in a patient considered to be free of disease at the time.

In contrast to the findings of Aristizabal and Caldwell,[1] and Schukovsky,[8] we were unable to separate recurrences, complications, and tumor control doses by comparing NSDs or total dose *vs.* time or number of fractions on Strandquist type plots. However, in the small subgroup of patients with supraglottic tumors and $T_4N_0M_0$ lesions, local control was obtained in 4 of 5 patients with radiotherapy alone, although marked edema and/or necrosis of the laryngeal cartilages were observed in 3 of the 4 (NSDs of 2,051, 2,261, and 1,921 rets). These data suggest that curative radiation therapy is possible in locally advanced supraglottic tumors, but that the mucosa and underlying cartilage are vulnerable when high dose radiotherapy is used. This is possibly due to the effects of decreased blood supply, hypoxia, infection and tissue destruction secondary to advanced local tumor growth.

Severe arytenoid and false cord edema occurred more frequently (5 of 27 patients with local control) at relatively low NSDs of 1,740–1,935 rets in patients with T_3 glottic tumors, who received larger primary radiation fields, than in those with Stage T_1 and T_2 lesions (3 of 90 with local control). Necrosis of the laryngeal cartilages, however, occurred only after the dose far exceeded 1,950 rets, at NSDs of 2,102, 2,137, 2,253, 2,260 and 2,435 rets (Table VII). An NSD value of 1,950 rets, equivalent to 6,600 rads in 30 fractions, given 5 times per week over 39 days, was considered to be near the normal laryngeal tissue tolerance at Stanford.

DISCUSSION

Laryngeal carcinoma, limited to T_1 and T_2 lesions of the true vocal cords only, is readily treatable by irradiation alone with an excellent chance of maintaining a useful post-therapy voice. In the Stanford series of T_1 and T_2 patients, only 1 of 99 died with uncontrolled tumor, and 8 of the 9 radiation failures were salvaged by laryngectomy. Local control was also obtained in over half of the patients with T_3 glottic tumors treated by irradiation alone and a majority of those patients were left with a useful voice. In addition, surgery following radiation therapy failure in the group with T_3 glottic carcinomas resulted in local control in 70 per cent of the patients with resectable lesions. An even higher percentage of locally controlled T_3 glottic tumors might be obtained by higher radiation doses (over 1,925–1,950 rets), but this is probably not feasible with the larger fields which are required to encompass these lesions because of the complications which occurred at NSDs of 1,740–1,935 rets in our series.

We were unable to correlate tumor differentiation or presenting symptoms with those patients who might benefit from an initial planned preoperative radiotherapeutic approach. Further randomized investigations in this direction should be considered, especially for those patients with advanced supraglottic lesions and clinically involved cervical lymph nodes, since the presence of lymphadenopathy in our series decreased the chances for local control with radiation therapy alone. In addition, the only 2 patients with supraglottic tumors and clinically positive cervical lymph nodes who had planned preoperative radiotherapy are alive without evidence of disease, as are 2 others without lymphadenopathy who also received planned preoperative irradiation. When the 8 patients with transglottic carcinomas and vocal cord fixation were considered separately, only 1 of the 4 radiation failures was resectable, making this the one glottic subgroup that should be considered for planned preoperative irradiation.

Supraglottic tumors without cervical lymphadenopathy, however, even though locally advanced, may be treated initially with radiation therapy. Seven of 9 patients with T_3 and $T_4N_0M_0$ lesions are alive with-

out evidence of disease, 6 of whom were treated only by radiotherapy. We believe that surgery should be reserved for radiation failures in this group.

In patients without clinically apparent cervical lymphadenopathy, large primary laryngeal fields were as effective in maintaining local control of tumor, as was the addition of a separate inferior cervical and supraclavicular port. However, this extra field may be important in patients with clinically evident involvement of cervical lymph nodes, and may be used without excessive morbidity in this situation. If radiation failure occurs, we have found that salvage may still be accomplished by neck dissection in approximately 60 per cent of the operable cases.

In conclusion, it is apparent that T_1 and $T_2N_0M_0$ glottic lesions are readily treatable by irradiation alone, with an excellent chance of maintaining a useful post-therapy voice. It is our opinion that patients with T_3 glottic carcinoma should also be irradiated primarily with curative intent, with laryngectomy to follow if radiation therapy fails. Preoperative radiotherapy should be considered; however, for the subgroup of patients with transglottic laryngeal tumor and a fixed vocal cord, since few of these patients were operable after radiation therapy failure occurred. Patients with small supraglottic primary tumors, as well as those with locally advanced carcinomas and negative necks (Stages T_3N_0 and T_4N_0) may also be irradiated with curative intent. Planned preoperative radiotherapy may be the treatment of choice in those patients with large supraglottic tumors and cervical lymph node disease, but randomized clinical trials are necessary to test this hypothesis.

SUMMARY

Two hundred and thirteen patients with carcinoma of the larynx were treated with the Stanford 4.8 mev. medical linear accelerator between 1957 and 1970. Included were 67 patients with supraglottic tumors and 146 with involvement of glottic structures. The 78 patients with carcinoma limited to a single true vocal cord had a 5 year actuarial survival of 90 per cent, with 4 of 5 radiation failures being salvaged by laryngectomy. There was only 1 tumor-related death in the 99 patients with T_1 and T_2 glottic lesions.

Local tumor control was achieved in approximately one-half of the patients with supraglottic tumors treated initially by irradiation alone, while surgery after irradiation failure resulted in local control in 12 of 15 patients with resectable lesions. An additional 4 patients with planned preoperative irradiation were also controlled locally and are alive without evidence of disease.

These cases are also analyzed according to presenting symptoms, complications, sites of metastases, quality of postirradiation voice, and results of concomitant cervical lymph node radiotherapy. Complications, recurrences and local control are also compared using the Nominal Standard Dose (NSD) concept.

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PERMANENT IMPLANTS IN THE MANAGEMENT OF HEAD AND NECK CANCER BY RADIOTHERAPY*

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AT THE 1960 meeting of the American Radium Society, Dr. Fernando Bloedorn and co-workers presented a paper titled, "The Place of Interstitial Gamma-ray Emitters in Radiation Therapy."[1] The introduction to this paper contained the following words: "The progress of radiation therapy in the last decade has been characterized by technical developments: the use of supervoltage, isotopes, moving field techniques and the application of more scientific dosimetry. At the same time very little has been done to develop further the techniques of interstitial irradiation which have proved to be so efficient in the treatment of a number of malignancies. The tendency in most radiation therapy centers is to abandon the use of radium in favor of external beam therapy even in cases where its efficiency has been proved by the good results obtained."

Now, 12 years later, the plea for continued use of interstitial gamma ray radiation therapy remains timely in drawing attention to a valuable means of curative radiation therapy. The advantages and disadvantages of radium and its replacement isotopes have been aptly described by Bloedorn *et al.*, as have the principles underlying the use of interstitial therapy in combination with external beam treatment. Among the patient histories described by these authors, the use of radon seeds in combination with external beam cobalt 60 teletherapy was mentioned for a patient with squamous cell carcinoma of the buccal mucosa, retromolar trigone and soft palate. At the American Oncologic Hospital, this method of treatment has been used successfully in a number of anatomic locations of head and neck squamous cell carcinomas in which a more conventional implantation with radium needles or substitutes is difficult or impossible.

It is the purpose of the present paper to describe our technique of permanent interstitial implantation of radon seeds in head and neck cancers, and to present the results of such treatment.

TECHNIQUE

We have used radon seeds exclusively because of their easy accessibility, reliable delivery and wide variety of activities. With suitable modifications, the use of radioactive gold or I^{125} seeds should be possible.

Radon seeds are delivered in form of precalibrated gold tubes containing radon gas (Fig. 1). They are usually used in activities from 0.10 to 3.0 millicuries per implant. We have designed a monitoring scale for a Geiger-Müller counter, with which the relative activity of each seed can be checked in the operating room and an occasional dud eliminated from implantation (Fig. 2). The actual implantation is usually carried out under endotracheal general anesthesia, using a variety of insertors with different angulations of the tip depending on the anatomic location (Fig. 3). Occasionally, implantation under local anesthesia or with nerve block is carried out.

DOSAGE

Our system of treatment in the tumors described here usually consists of external beam cobalt 60 teletherapy for a dose of 5,000 rads to the primary tumor and immediate lymph node bearing area. Depend-

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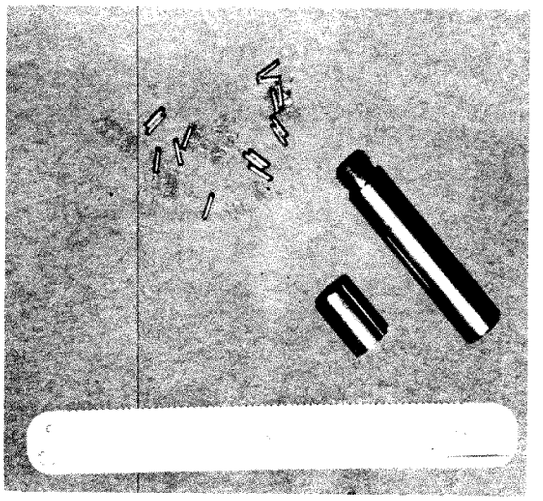


Fig. 1. Radon seeds.

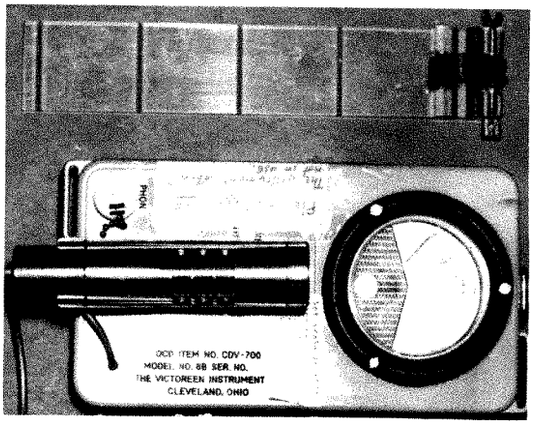


Fig. 2. Monitor for radon seeds.

ing upon the location of the tumor, parallel opposing portals, a unilateral single portal, or a pair of wedges are used. After completion of this series of external beam therapy, the acute reaction is allowed to subside and the patient is evaluated regarding the risk of general anesthesia. All patients with squamous cell carcinomas of the soft palate, uvula, tonsillar area, retromolar trigone, palatoglossal sulcus and with lesions of the posterior pharyngeal wall are considered for combined external beam and interstitial radon seed implantation regardless of the extent of their disease in the cervical lymph nodes, because the reason for failure of treatment in these patients is usually failure to control the primary tumor or the tumor in the cervical lymph nodes, or both. Lymph node metastases are handled either by radiation therapy only, using a combination of external beam and interstitial radium implantation, or by external beam therapy and subsequent neck dissection. Patients are only excluded from the combined external and interstitial treatment plan if they are not suitable for general

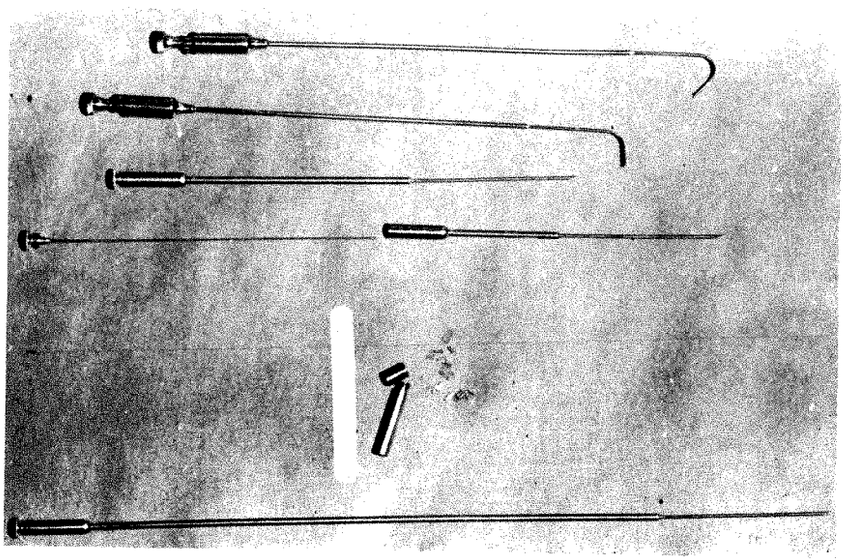


Fig. 3. Insertors for radon seeds.

anesthesia on the basis of associated medical conditions, such as electrocardiographic abnormalities, chronic pulmonary disease and cirrhosis of the liver which would present an undue anesthesia risk, or occasionally because of distant metastases.

The implantation is designed to deliver an additional dose of 2,000 to 3,000 r to the primary tumor bearing area, with the activity of the individual radon seed implants determined on the basis of a plan of implantation, which follows Paterson-Parker rules[9] wherever possible. In general, the seeds are ordered with an intensity of approximately 0.2 millicuries per implant. The total dose in the primary tumor bearing area therefore reaches a minimum dose of 7,000 rads and a maximum of 8,000 rads.

REPORT OF CASES

CARCINOMA OF THE SOFT PALATE

Case 1. J.M., a 61 year old male, presented with squamous cell carcinoma of the soft palate, Stage $T_3N_0M_0$[2] (Fig. 4). Five thousand rads

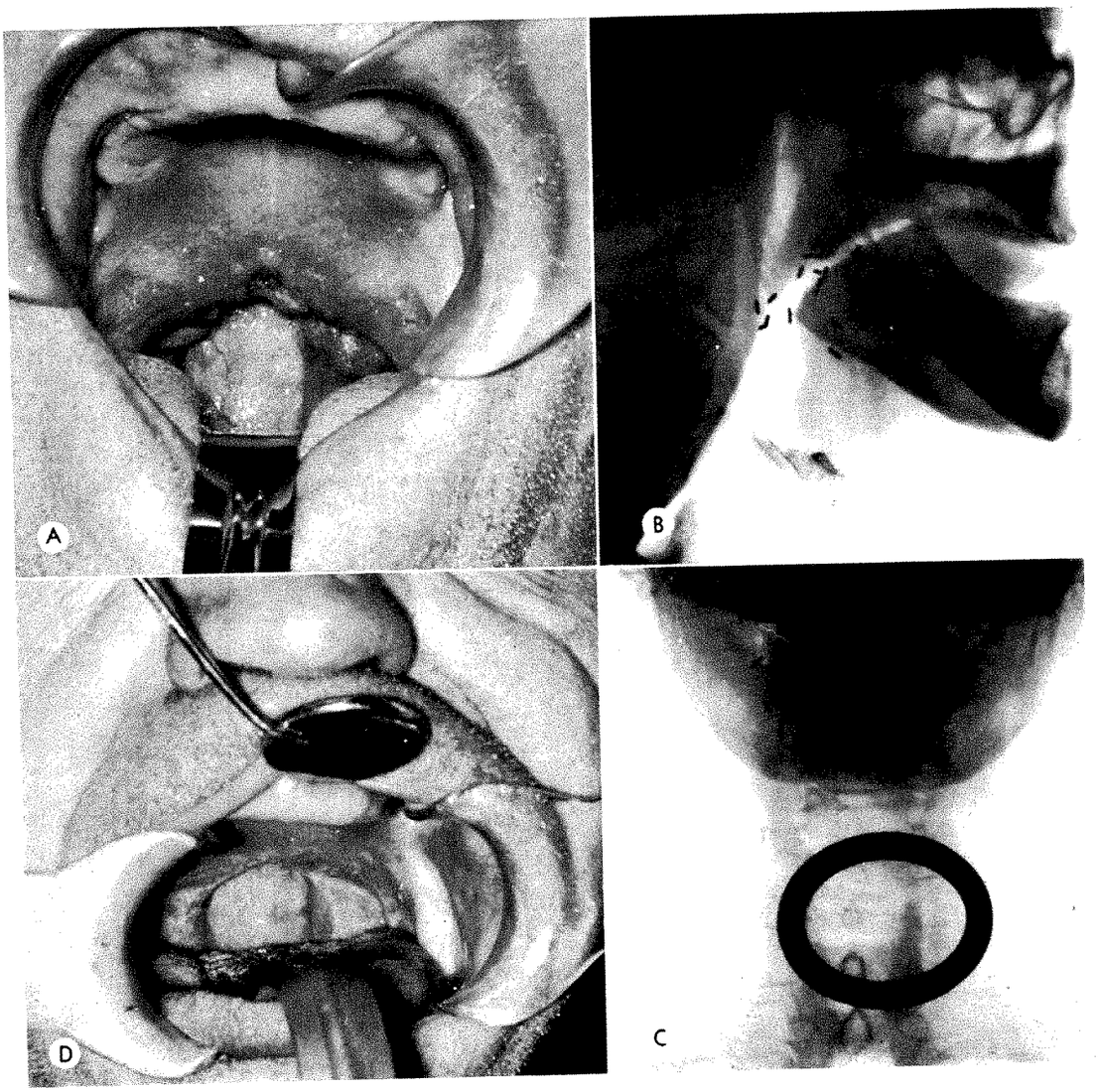


Fig. 4. Case 1. Carcinoma of the soft palate.
(*A*) Before treatment. (*B* and *C*) Radon seed implant. For details see text. (*D*) After treatment.

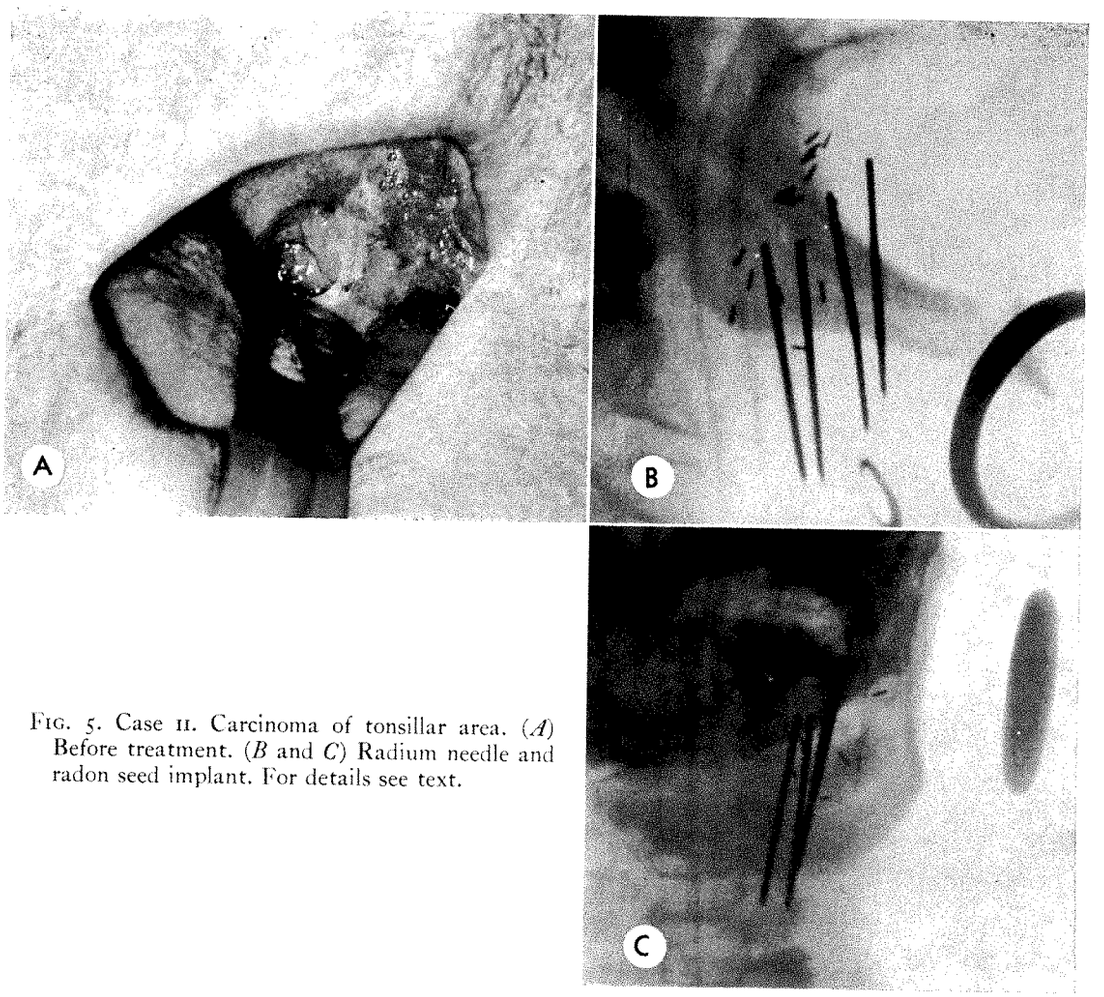


Fig. 5. Case II. Carcinoma of tonsillar area. (*A*) Before treatment. (*B* and *C*) Radium needle and radon seed implant. For details see text.

midline tumor dose were delivered in 38 days using parallel opposing cobalt 60 teletherapy portals. Eleven days following the end of the external beam therapy, 27 radon seeds of 0.22 millicuries each were implanted in the soft palate, tonsillar fossae and posterior and anterior tonsillar pillars. A minimum tumor dose of 2,200 r and a maximum tumor dose of 2,700 r from the radon seed implant was calculated at 0.5 cm. distance from the implant.

The patient is free of local disease and metastatic lymph nodes 19 months following completion of treatment.

Carcinoma of the Peritonsillar Area

Case II. W.D., a 76 year old male, presented with squamous cell carcinoma of the left tonsillar fossa, Stage $T_2N_0M_0$,[3] and received 5,000 rads tumor dose in 32 days at the lateral margin of the tongue from a single lateral cobalt 60 portal including the adjacent upper neck lymph nodes (Fig. 5). Twelve days following the end of cobalt irradiation, a radon seed implantation was carried out using 21 radon seeds of 0.2 millicuries each to the lateral soft palate, the tonsillar fossa and the anterior and posterior tonsillar pillars. Four radium needles were inserted in the adjacent area of the tongue. The dose calculated from the radon seeds gave a minimum of 2,100 r and maximum of 2,700 r; the radium needles delivered a dose of 2,000 r in 57 hours at 0.5 cm. distance, calculated according to Quimby.[6]

The patient is free of local and metastatic disease 27 months following the end of his radiation therapy.

Case III. H.C., a 68 year old female, was seen with trismus due to a squamous cell carcinoma

involving the right soft palate, anterior tonsillar pillar, palatoglossal sulcus and the right posterior mobile tongue and base of the tongue (Fig. 6). She was staged $T_3N_1M_0$ because of lymphadenopathy palpated in the right submandibular region and in the right mid neck. Trismus did not allow an adequate photograph at the beginning of treatment which consisted of external beam cobalt 60 teletherapy with parallel opposing portals for 5,000 rads in 35 days to the primary tumor and the upper neck. The low neck received 5,000 rads given dose from a separate anterior portal. Eight days later, 20 radon seeds of 0.2 millicuries intensity were implanted in the right soft palate, the peritonsillar region and the right retromolar trigone. A volume implant using half intensity radium needles was carried out in the tongue, following Paterson-Parker rules, as well as 2 single plane implants of the lymph nodes in the right submandibular and right cervical areas. The dose delivered 0.5 cm. from the radon seed implant was calculated as between 2,500 and 3,300 r, the dose to the tongue was 2,000 r and the dose to the neck nodes was 2,500 r at 0.5 cm.

The patient has been free of tumor for 40 months following her treatment.



Fig. 6. Case III. H.C., carcinoma of tonsillar area, for details see text. Radium needle and radon seed implant was used.

After treatment. The ulceration has since healed.

Carcinoma of the Posterior Pharyngeal Wall

Case IV. E.B., a 77 year old male, presented with a squamous cell carcinoma, posterior pharyngeal wall, with right cervical lymphadenopathy, staged $T_3N_2M_0$ (Fig. 7). Cobalt 60 teletherapy was administered to the primary tumor bearing area and the upper neck to a midline tumor dose of 5,000 rads in 44 days using parallel opposing portals. Ten days following the end of this series of external beam therapy, 16 radon seeds of 0.17 millicuries each were implanted in the posterior pharyngeal wall

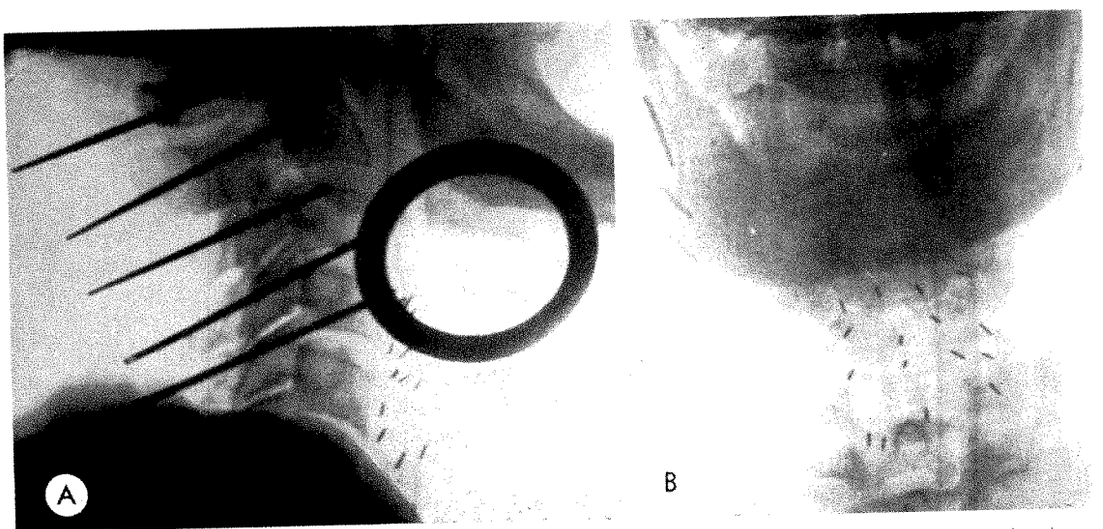


Fig. 7. Case IV. (*A* and *B*) Carcinoma of posterior pharyngeal wall, radium needle and radon seed implant.

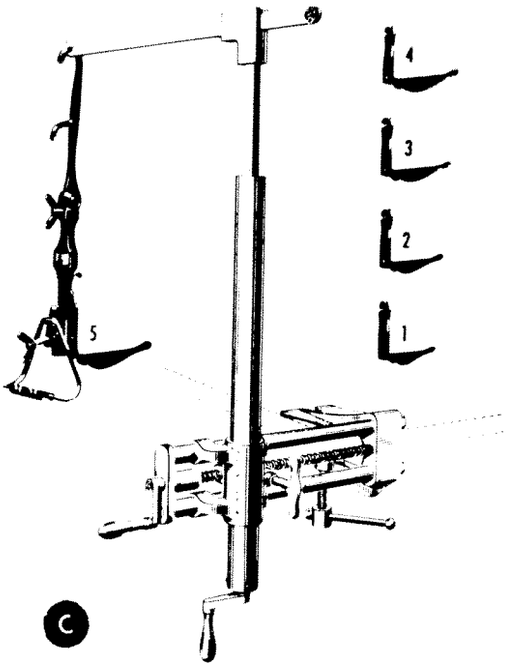


Fig. 7. (*C*) Lynch suspended laryngoscope.

using a Lynch suspended laryngoscope (Fig. 7*C*), for a dose of 2,300 to 3,200 r. In addition, 5 full intensity radium needles were inserted in the right neck for an additional dose of 2,500 r at 0.5 cm. from a single plane in 48 hours. The patient is now 8 months following the end of his radiation therapy, with no evidence of residual or recurrent tumor in the posterior pharyngeal wall or in the neck lymph nodes.

He recently developed lung metastases which are being treated by chemotherapy.

Carcinoma of the Buccal Mucosa

Although temporary implants using radium needles or their substitutes are usually preferred in lesions with involvement of the buccal mucosa, extension of the tumor into the gingival buccal sulcus or into the region of the retromolar trigone may be more suitable for permanent implantation because of their difficult anatomic surfaces.

Case v. H.P., a 71 year old male, had a squamous cell carcinoma involving the right buccal mucosa, upper and lower gingivobuccal sulcus, retromolar trigone and the upper gingiva with extension to the soft and hard palate, Stage $T_3N_0M_0$ (Fig. 8). The patient was initially treated with a pair of wedges using cobalt 60 teletherapy for a dose of 6,000 rads in 45 days. Following subsidence of the acute reaction, an applicator was built and loaded with 40 mg. of radium in tubes for treatment of the extension of the tumor to the hard palate. This delivered a dose of 1,500 r at the mucosa in 2 applications of 3 hours each. Thereafter, under endotracheal general anesthesia, a radon seed implantation was carried out using a total of 35 radon seeds of 0.24 millicuries each to the remaining primary tumor bearing area. The relationship of this implant to the radium treatment was established by application of the mold with dummy sources in the operating room. Also, 4 half-intensity radium needles were implanted in the lateral margin of the tongue. The dose delivered from the radon seed implant was calculated as between 1,800 and 2,300 r, and 1,000 r in 14 hours were delivered by the radium needles at 0.5 cm. distance. A review of the radon seed implantation revealed an area of poor placement, and after subsidence of the acute reaction, an additional 5 sources of 0.2 millicuries each were inserted under local anesthesia in an area of poor mucosal reaction. One month later a few suspicious nodules in the retromolar trigone were coagulated.

The patient has been free of local tumor and metastatic malignancy in the neck or in distant sites for 1 year.

Case vi. D.K., who presented with a squamous cell carcinoma of the right upper gingiva, extending to the gingival buccal sulcus and hard palate, Stage $T_3N_0M_0$, is an example of the use of radon seeds in an unusual fashion (Fig. 9). The patient was a male 82 years of age, with a poor anesthetic risk. He was initially treated with a pair of wedges using cobalt 60 teletherapy for a dose of 5,000 rads in 34 days. An applicator was then made to fit the patient's right upper gingival buccal sulcus and adjacent structures, and 21 radon seeds of 2.05 millicuries each were inserted in holes of 0.7 cm. depth. The patient applied the mold on 3 days, for 8 hours each, during which a dose of 2,000 r, 0.5 cm. from the surface of the applicator, was administered.

The patient has been free of recurrent or residual tumor in the primary tumor bearing area, and free of metastatic disease for 24 months.

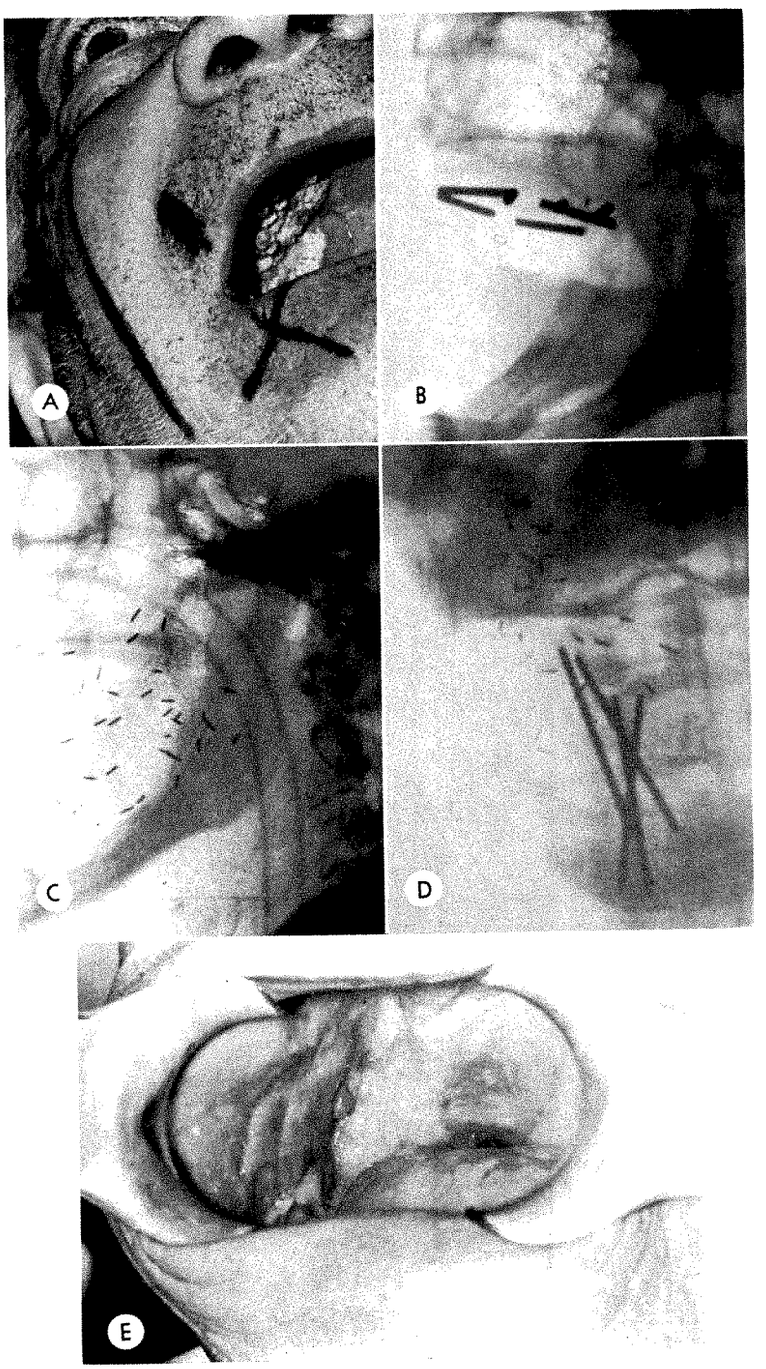


FIG. 8. Case v. H.P., carcinoma of buccal mucosa and adjacent area.
(*A*) Before treatment. (*B*) Lateral roentgenogram of radium mold. (*C*) Lateral radon seed implant. For details see text. (*D*) Anterior roentgenogram of radon seed and radium needle implant. (*E*) After treatment.

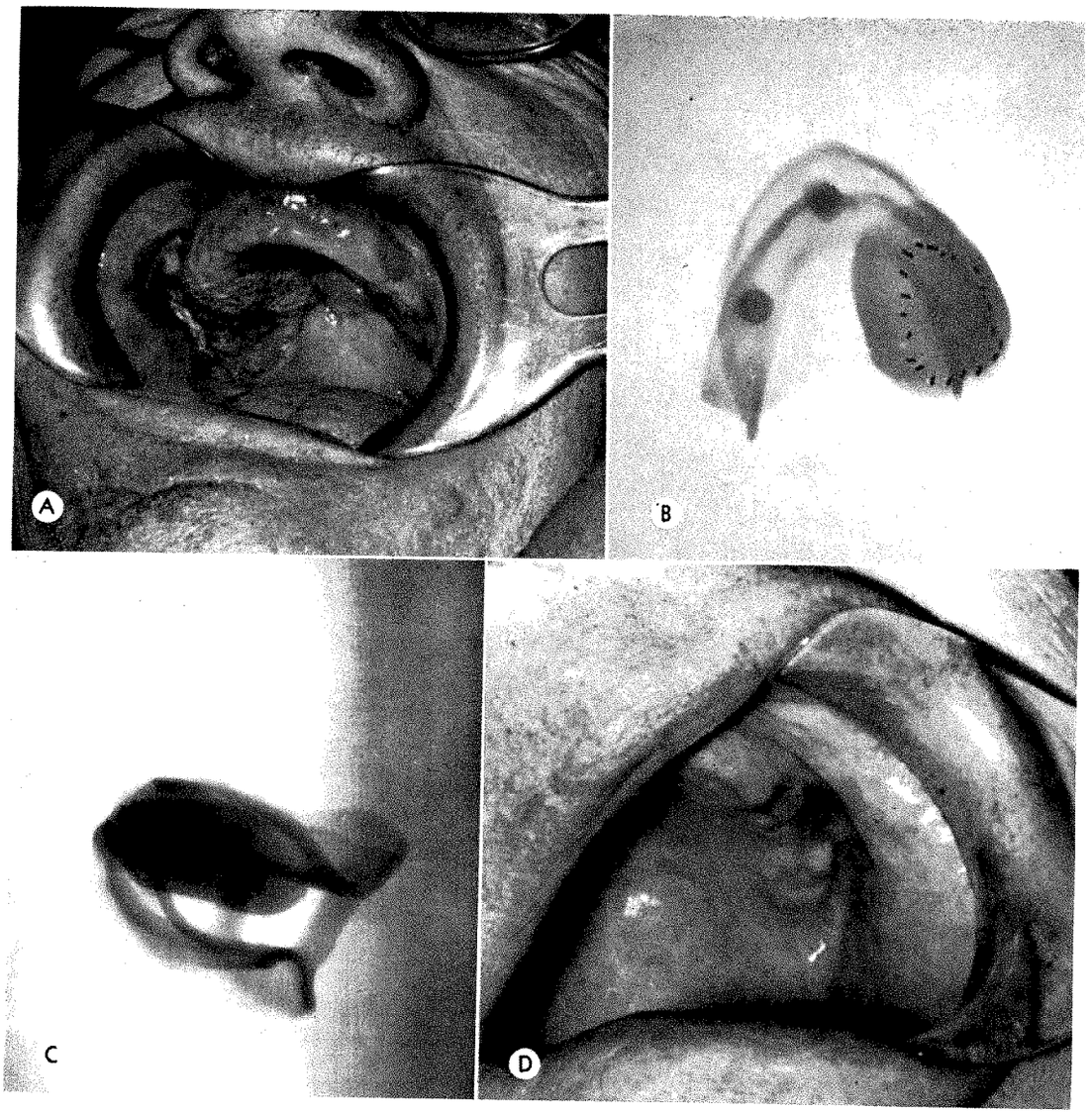


FIG. 9. Case VI. D.K., carcinoma of gingiva.
(*A*) Before treatment. (*B* and *C*) Applicator with radon seeds. For details see text. (*D*) After treatment.

RESULTS OF TREATMENT

The classification of the patients treated by radon seed implantation in a 3 year period is given in Table I. Of 21 patients treated 6 months or more ago, 18 have local control of the primary site. In 1 patient, who was described above, coagulation of a suspected small recurrence has produced local control. One patient with a cancer of the tonsillar area had a marginal recurrence 10 months following treatment and is being considered for surgery. One patient refused a second implant and has since undergone surgery for a recurrence. Complications in form of soft tissue necrosis occurred in 3 patients, but healed completely after conservative treatment for a number of weeks. In 1 patient with an extensive tumor of the tonsillar area involving the pyterygopalatine fossa, sequestrectomy was re-

quired for osteonecrosis of the mandible and trismus has been a problem. Neck lymph nodes were treated by radical radiation therapy in 6 patients, 5 of whom had a positive lymph node biopsy. In 3 patients the lymph nodes have been controlled for 12 to 35 months, and in 2 patients residual tumor was found during a neck dissection.

Table II summarizes the experience as regards control of the primary tumor. The occurrence of distant metastasis in patients with advanced cervical lymphadenopathy and relatively frequent death from intercurrent disease have been described by others in the past.[4]

Review of the result of treatment of similar lesions at the American Oncologic Hospital since 1925 by a number of radiation therapists revealed that among 4 patients treated by megavoltage radiation therapy for carcinoma of the buccal mucosa, 2 had local control for 1 year or more. In 6 selected patients treated by peroral roentgen ray cone, 5 had local control, and among 6 patients treated by interstitial implantation, 4. Fifty-six more patients were treated for tumors which were too advanced for radical treatment or by external orthovoltage roentgen therapy only.

Of 16 patients treated by megavoltage radiotherapy for carcinomas of the posterior pharyngeal wall, 31 per cent had local control. Fourteen patients were treated either for palliation or by orthovoltage roentgen therapy only.

Among 61 patients treated for carcinoma of the tonsillar area using supervoltage radiotherapy, 43 per cent had local control, while among 43 selected patients treated by peroral roentgen ray cone, 65 per cent were free of tumor at 1 year. An additional 111 patients were only partially treated or managed using external beam orthovoltage roentgen therapy.

TABLE I

RADON SEED IMPLANTS
CONTROL OF PRIMARY LESION BY RADIOTHERAPY

Site	6–12 Months	12–24 Months	over 24 Months
Gingiva (1 patient)		1	
Buccal mucosa (2 patients)	*	1	
Soft palate (5 patients)	2	2	1
Posterior pharyngeal wall (4 patients)	2	1	1
Tonsillar area (9 patients)	2	3	2

* One patient controlled by coagulation of residual tumor.

TABLE II

LOCAL FAILURE AND CAUSE OF DEATH

Buccal mucosa (2 patients)	1-residual tumor, controlled by coagulation
Posterior pharyngeal wall (4 patients)	1-died, 8 months, of intercurrent disease 1-died, 10 months, of neck metastasis
Tonsillar area (9 patients)	1-died, 15 months, of distant metastasis 1-died, 2 months, of automobile accident 1-refused second implant, controlled by radical surgery 1-marginal recurrence-surgery

SUMMARY

The results of treatment of carcinoma of the buccal mucosa, gingiva, tonsillar area and posterior pharyngeal wall using permanent interstitial implantation are reported.

In spite of the fact that many of the lesions were locally advanced, this method of treatment offered an effective means of controlling local tumor.

For patients with adequate operative risk, the combination of external beam megavoltage therapy and interstitial implantations offers a better rate of local tumor control than external beam radiation therapy alone.

Interstitial gamma-ray therapy may be used even when the indications are unusual, and good results may be obtained

with a minimum of late changes and undue complications.

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APPLICATIONS OF THE ELECTRON BEAM IN THE MANAGEMENT OF THE LYMPHATICS OF THE NECK IN HEAD AND NECK CANCERS*

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THE physical characteristics of the megavoltage electron beam are[9]: (1) relatively high surface dose (calculated to be from 83 to 90 per cent for energies from 6 to 12 mev. and more than 90 per cent for 15 and 18 mev.); (2) steep build up to maximum dose; (3) sharp fall-off in dose after 80 per cent dose level; and (4) selection of depth of tissue included in the high dose zone by varying the energy. These characteristics permit ideal irradiation of the cervical lymphatics in a multiplicity of clinical situations.

The most common clinical situations are:

1. Irradiation of one entire neck as the sole modality of elective treatment
2. Irradiation of one entire neck after radical neck dissection
   a. as elective treatment
   b. for recurrent disease
3. Irradiation of the spinal accessory chain of lymph nodes
4. Irradiation of extensions of surgical scars which cannot be included in the treatment field easily when postoperative treatment is given with the photon beam
5. Additional local dosage ("boost" therapy) after photon irradiation of residual masses or areas of high risk of infestation.

IRRADIATION OF ONE ENTIRE NECK

NO NECK DISSECTION

Elective treatment to the whole neck, with or without later neck dissection, is given with the electron beam when there is a high risk of lymphatic infestation which is limited to one side. This may be seen in the lateralized lesions of skin cancer, major salivary gland tumors, and squamous cell carcinomas of the buccal mucosa and gingiva. Treatment may be given to the neck in conjunction with treatment of primary lesion or the site of the primary lesion if excision has been done. For example, after removal of a malignant tumor of the parotid gland, if there is known or suspected residual disease and if the tumor is of high grade malignancy, the parotid area is irradiated with combined photon and electron beams and the entire ipsilateral neck is treated with the 9 or 12 mev. electron beam (Fig. 1).

With a clinically negative neck the given dose is 5,000 rads in 4 weeks or 5,500 rads in $4\frac{1}{2}$ weeks; this provides a dose to the lymphatics in the range of 4,500 to 5,000 rads. Similar treatment may be provided for an oral cavity lesion with a clinically suspicious lymph node. A planned radical neck dissection is done after the radiation therapy is completed. A series of reviews of patients with cancers of the upper respiratory and digestive passages treated at the M. D. Anderson Hospital has demonstrated that 4,500 rads in 5 weeks to 6,000 rads in 6 weeks effectively prevents the appearance of nodal disease in the clinically negative neck.[1–3,6,7]

AFTER NECK DISSECTION

In the operated neck, the treatment field must include all extensions of the surgical scar. This can present difficulties, particularly when the anterior limb of the neck incision extends directly across the thyroid cartilage. It is then necessary for the larynx to remain in the field without shielding until at least 4,500 rads have been

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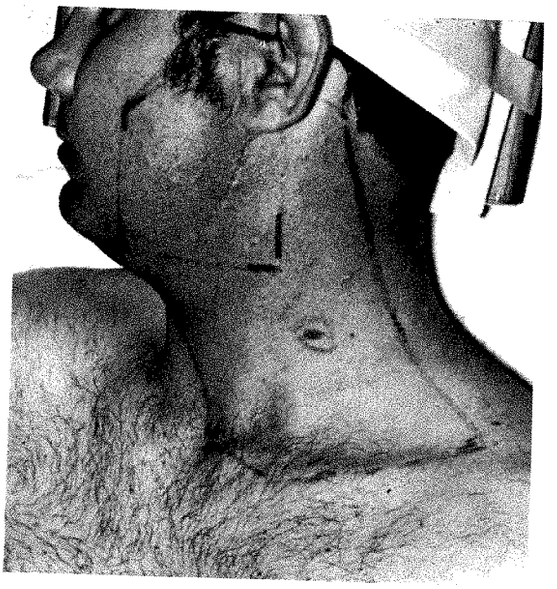


FIG. 1. This 37 year old male was referred to M. D. Anderson Hospital for radiation therapy in February 1972 after a total parotidectomy for high grade mucoepidermoid carcinoma of the left parotid gland. Sacrifice of the 7th nerve was necessary since the tumor was wrapped around it. Because of nerve involvement and the relatively undifferentiated tumor, radiation therapy was recommended for the parotid bed area and for the entire ipsilateral neck.

The parotid area was treated with a single left lateral 10×8 cm. portal, using 18 mev. electron and photon beams in a 1:1 ratio of given doses. In 5 weeks, the patient received 5,000 rads at a depth of 5 cm. to the large field and an additional 500 rads with the photon beam through a small field limited to the base of the skull. The entire neck was treated with 11 mev. electrons to a given dose of 5,000 rads in 4 weeks. The neck field was defined with a lead cut-out. The patient developed mild hoarseness and had marked throat soreness when the given dose to the neck had reached 3,750 rads in 3 weeks. There was minimal ipsilateral laryngeal edema and exudate along the lateral pharyngeal wall.

Electrons of 11 mev. had been selected because of the thickness of the soft tissues in the neck, since there had not been a neck dissection. The resulting depth dose produced intense mucosal reactions. The electron energy was decreased to 9 mev. for the remainder of the treatment and the severity of the mucosal reaction subsided.

The patient is shown in treatment position with the treatment fields defined for the parotid bed area and for the entire neck. The surgical scar can be seen in the pre-auricular area and extends from the subdigastric area upward behind the ear.

given. If possible, 6 mev. is used which will limit the dose to the ipsilateral laryngeal structures. If the scar crosses the midline into the opposite neck and if there is high risk of contamination of this portion of the surgical wound, a small appositional field is used to cover this scar. The same treatment technique can be used for the patient who has had bilateral radical neck dissection. Every effort must be made to shield the larynx throughout treatment since the patient probably already will have some edema of the arytenoids from the surgery.

Elective Treatment. The indications for treatment of the whole neck after radical neck dissection are: (1) many positive lymph nodes in the surgical specimen; (2) total replacement of a lymph node by tumor or rupture of a cystic lymph node; (3) tumor found in connective tissue; and (4) tumor found in the perineural lymphatics.

Healing must be complete before irradiation is started, usually 14 to 21 days after surgery. If the flaps are very thin, the entire neck may be treated at 6 mev.; with thicker flaps 9 mev. is necessary (Fig. 2). When there are large, partially fixed or fixed lymph nodes which have been removed from the upper neck or if the involved lymph nodes were attached to the periosteum of the mandible, the neck field is divided with the upper neck being treated at 9 to 15 mev. and the lower neck being treated at 6 mev. (Fig. 3). The larynx is included in the lower portion of the field and is irradiated with the lower mev. which sharply diminishes the dose to the contralateral laryngeal structures. The given dose will be 5,000 rads in 4 weeks or 6,000 rads in 5 weeks except in patients with extensive fixed lymph nodes who require a boost field to the area. An additional 1,000 to 1,500 rads may be given through a sharply reduced field.

Recurrent Disease. Treatment may be given with the electron beam for recurrent disease. Recurrent disease may present as small cutaneous nodules or as an in-

filtrative mass and usually is located close to the neck dissection scar. With recurrent disease, the given dose will be higher, usually 6,000 rads in 5 weeks to the whole involved neck with 1,000 to 1,500 rads added dose to the site of recurrence through a reduced field. With a planned high dose,

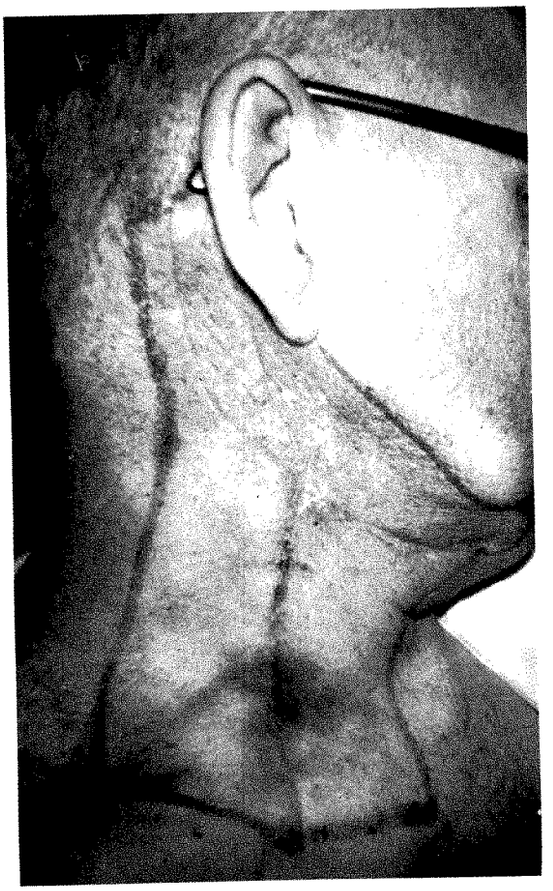


FIG. 2. This 62 year old male was first seen at the M. D. Anderson Hospital in April 1964 with a scar 12 cm. long in the right cervical region from removal of an enlarged lymph node, reported to be undifferentiated carcinoma. There was the suggestion of a mass in the lower jugular area. No primary lesion could be found after extensive search and multiple mucosal biopsies.

On May 5, 1964, a right radical neck dissection was done. Metastatic unclassified carcinoma was found in 2 of 9 subdigastric lymph nodes and in connective tissue in the subdigastric region. No tumor was found in the middle or lower jugular lymph nodes. In 5 weeks, the entire dissected neck received 5,000 rads given dose with 12 mev. electrons plus 1,000 rads given dose with 9 mev. electrons. The patient showed no evidence of disease in September 1971. The tissues were in excellent condition 7½ years after surgery and radiation therapy. (Courtesy: *Current Problems in Radiology*.[5])



FIG. 3. This 64 year old male was first seen at the M. D. Anderson Hospital in June 1966 with a history of having had a radium needle implant in July 1965 for carcinoma of the lower lip. In March 1966, the lip lesion recurred. On examination, as well as the recurrence on the lip, the patient had a mass overlying the left mental foramen. The recurrent lip lesion was resected and a left radical neck dissection done. The pathology report described squamous cell carcinoma, Grade II. In the neck, 6 of 51 lymph nodes contained tumor deposits and tumor was found in the connective tissue.

The patient received postoperative irradiation to the entire neck with the electron beam. The upper portion of the field overlying the mandible (measuring 6×10 cm.) was treated to a given dose of 6,500 rads in 5½ weeks with 15 mev. The remainder of the neck, including the mastoid tip, was treated with 9 mev. to 6,000 rads given dose in 5 weeks.

The patient showed no evidence of disease in June 1971. The irradiated tissues are in good condition, soft and pliable on palpation, 5 years after completion of treatment.

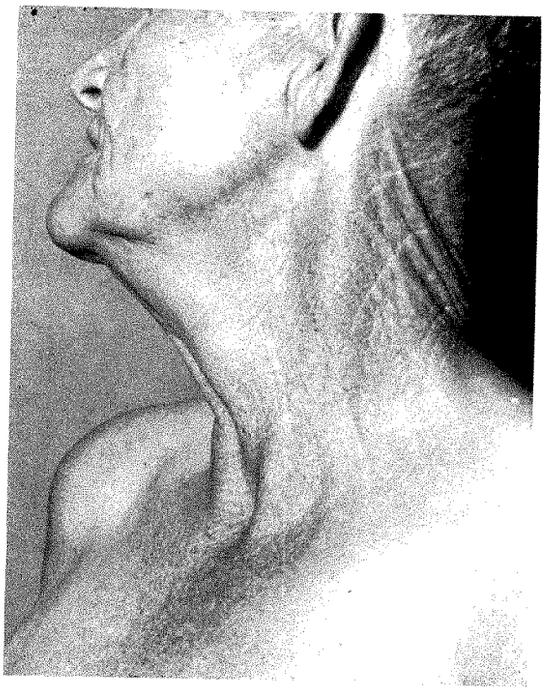


FIG. 4. This 61 year old male, first seen at the M. D. Anderson Hospital in 1966, had a history of skin cancers of the face treated by excision and radium several years previously. He developed a mass in the left upper neck which extended into the superficial lobe of the parotid. A partial parotidectomy was performed, but no attempt was made to resect the entire tumor. The tumor was reported to be poorly differentiated squamous cell carcinoma with extensive invasion of the perineural lymphatics. When the patient was seen for radiotherapy, there was a firm mass anterior to the ear and induration in the upper neck.

Treatment was given to the parotid area with combined 18 mev. photon and electron beams. In 6 weeks, the dose was 6,000 rads at 5 cm. depth. The entire neck was treated with the 9 mev. electron beam, giving 6,000 rads in 5 weeks. In November 1971, 68 months later, the patient was well and the irradiated tissues were in excellent condition.

The patient is shown $6\frac{1}{2}$ years later with essentially normal appearing tissues, except for some scarring at the site of the radium treatment for a previous skin cancer in the left cheek.

it is essential to shield the larynx when 4,500 rads has been given. If the recurrent disease is in the vicinity of the laryngeal structures, a lucite block 1 or 2 cm. thick can be placed over the larynx to decrease the depth dose. If the recurrent mass is thick, 12 to 15 mev. electrons may be necessary.

Complications. With electron beam irradiation to the whole neck, the acute reaction is a brisk erythema followed by dry desquamation. When the given dose is more than 5,500 rads in $4\frac{1}{2}$ weeks, patches of moist desquamation usually are seen in the high dose areas, but healing occurs in 7 to 10 days. Moderate pharyngeal mucositis usually occurs, producing some discomfort on swallowing. An occasional patient will develop hoarseness due to an undesirably high dose to the laryngeal structures when shielding cannot be used. The reaction in the larynx is almost always minimal and edema of the laryngeal structures is limited to the ipsilateral side. In the unoperated neck, fibrosis does not develop and skin changes are minimal (Fig. 4). In the operated neck, there may be minimal to moderate subcutaneous fibrosis, but significant fibrosis has been infrequent. It has been seen only in patients who have had a radical neck dissection with very thin skin flaps and with a trifurcate incision. Telangiectasias may occur but are infrequent unless the given dose has exceeded 6,000 rads.

RESULTS OF IRRADIATION AFTER RADICAL NECK DISSECTION

Seventy-five patients have received electron beam treatment to one entire neck, and to both necks in 6 patients, from May 1963 through December 1969. Treatment has been given electively after radical neck dissection has been performed for extensive neck disease or for recurrent disease in the neck occurring 2 to 26 months after radical neck dissection. Freedom from recurrence of disease has been achieved most often in those patients without gross disease who have been treated electively. Table 1 shows that 11 of 31 patients receiving elective irradiation after neck dissection are alive with no evidence of disease up to 8 years after treatment and that 9 patients have died from intercurrent disease or distant metastases, free of disease above the clav-

Table I

RESULTS OF ELECTRON BEAM TREATMENT
CERVICAL LYMPHATICS

(May 1963–December 1969; reviewed April 1972)

	Elective Treatment After Radical Neck Dissection	Treatment for Recurrence After Radical Neck Dissection
Total Patients	31	16
Alive and No Recurrence of Neck Disease	11	2*
Dead and Free of Disease Above the Clavicle	9 4 died from DM† 5 died from intercurrent disease	6 3 died from DM†
Dead with Recurrence of Neck Disease	11 5 outside field 6 within field 6 died with DM†	8 4 within field 4 within + outside field 4 died with DM†

* One patient developed a recurrence within the field which was removed by cryosurgery, with no further recurrence.
† DM = distant metastasis.

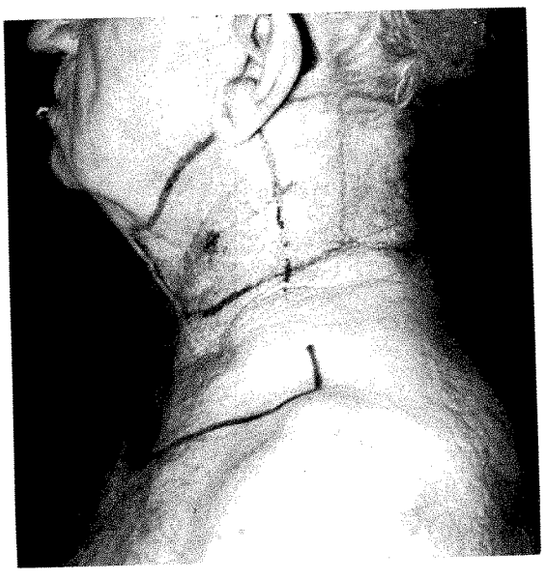


Fig. 5. This 70 year old man was seen in March 1970 with a recent biopsy scar in the right subdigastric area surrounded by induration. There was a 2.5 cm. node in the left midjugular area. The posterior aspect of the suprahyoid epiglottis was thickened and distorted and biopsy showed squamous cell carcinoma. The lymph node histology was poorly differentiated squamous cell carcinoma. The patient's disease was staged T_1N_{3B}.

From April 2, 1970 to May 20, 1970 the primary lesion received 6,600 rads with parallel opposing Co^{60} fields and the lower necks received 5,000 rads given dose. After 4,500 rads tumor dose the primary treatment portals were reduced to exclude the spinal cord. The 6 mev. electron beam was used to treat both posterior cervical lymph node areas to bring the minimal tissue dose to 5,500 rads.

Approximately 6 weeks after completion of the irradiation, simultaneous modified bilateral neck dissections were done with excision of the scar in the right neck. The sternocleidomastoid and anterior jugular vein were not removed. Of 22 lymph nodes recovered from the right neck, 5 showed necrotic tissue with peripheral fibrosis and focal cholesterol slits consistent with degenerative cancer. From 35 lymph nodes recovered from the left modified neck dissection, 1 contained necrotic tissue with peripheral fibrosis and inflammation consistent with degenerative metastasis. No viable tumor was identified in any of these specimens. The patient was seen in March 1972 with no evidence of disease.

The patient is shown after the upper fields have been moved forward to exclude the spinal cord and the posterior strip field has been defined for electron beam treatment. (Reproduced from: Fletcher, G. H., *Textbook of Radiotherapy*.[4])

icle. Of 16 patients receiving treatment for recurrent neck disease, only 1 patient has remained alive free of local or generalized disease. More than half the patients have



Fig. 6. This 68 year old male was admitted in June 1971 with a history of rapidly enlarging upper neck lymph nodes. The patient had multiple semi-fixed lymph nodes in the posterior cervical, subdigastric and midjugular regions, and a mass in the parotid gland. A complete parotidectomy with sacrifice of the 7th nerve and a left radical neck dissection were done. The pathology diagnosis was high grade mucoepidermoid carcinoma with infestation of 25 of 26 cervical lymph nodes. Carcinoma had invaded the connective tissue and muscle.

Postoperative treatment was given to the parotid bed and upper neck with parallel opposed Co^{60} portals with a 2:1 loading favoring the left. The midline tumor dose was 6,000 rads in 7 weeks at a weekly tumor dose of 850 rads. The area of scar in the left posterior neck received 5,280 rads at 1 cm. depth and was given 800 rads with 6 mev. electrons to increase the dose to 6,000 rads. The right spinal accessory chain required 650 rads with the 6 mev. electron beam for a total dose of 5,000 rads at 1 cm. Within a few months the patient had evidence of extensive disease throughout the deeper structures of the neck and distant metastases.

The treatment fields on the left are shown. The upper posterior rectangular field is the posterior strip which is being treated with the electron beam. It covers the mastoid tip and extends down to the superior margin of the lower anterior cervical Co^{60} field.

had recurrence of disease both within and adjacent to the treated neck even though higher doses had been given, and the areas of recurrent disease had been boosted to 7,000 or 8,000 rads.

Strong[8] reported on a controlled study of preoperative irradiation and radical neck dissection. In 204 patients who did not receive preoperative irradiation, a cervical recurrence rate of 54 per cent was found in the radically dissected neck of those pa-



Fig. 7. This 52 year old male was admitted in April 1970 with a 1.2 cm. slightly raised and ulcerated area on the right side of the undersurface of the tongue with good oral mobility. The clinical staging was T_1N_0. The patient gave a history of numerous attacks of sialadenitis in the submaxillary glands.

In April 1970, the tongue lesion was widely excised and primary closure was done. Six months later sudden swelling developed over the left submaxillary gland which regressed with antibiotics and probing the submaxillary duct. One month later the gland again became enlarged and tender. After adequate treatment with antibiotics, the gland was removed. There was an acute and subacute chronic sialadenitis with a small focus of squamous carcinoma in a lymph node overlying the gland.

Because the metastasis had appeared in the contralateral side, there was significant risk of new disease in the ipsilateral neck and 5,500 rads were given to the upper necks through parallel opposing portals and 5,000 rads in 5 weeks were given to the lower necks. A boost of 1,000 rads was given to the area of the scar in the left submental region through an appositional 7×12 cm. field with 9 mev. electrons. The patient shows no evidence of disease 2 years later.

The patient is shown with the head turned to demonstrate the electron beam appositional portal which is only slightly smaller than the left upper neck field.

tients who had positive lymph nodes. The recurrence rate was 71 per cent in patients with lymph nodes positive at multiple levels. It is for the purpose of preventing this anticipated high rate of recurrence after neck dissection that radiation therapy, done ideally with the electron beam for the single neck, is given when many lymph nodes are positive or when tumor is found in connective tissue.

TREATMENT TO SPINAL ACCESSORY CHAIN LYMPH NODES

Irradiation of the spinal accessory chain nodes is indicated in a variety of situations. If the primary lesion is treated with paral-

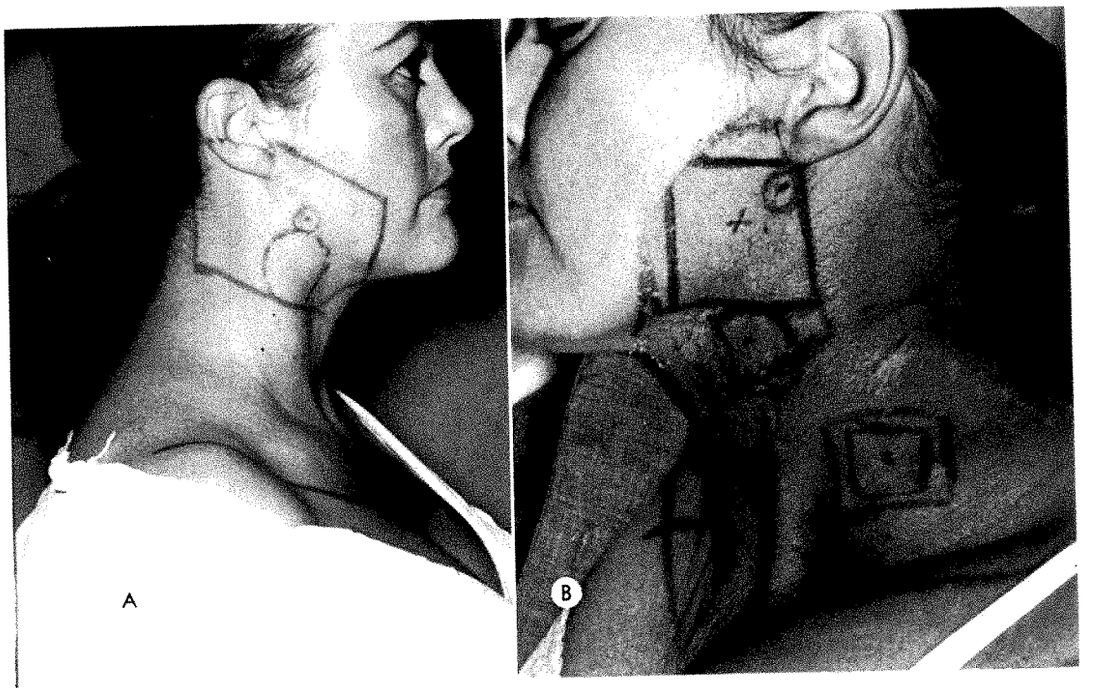


FIG. 8. (*A* and *B*) This 43 year old female was first seen in July 1970 with a 2 cm. squamous cell carcinoma with spindle component of the base of the tongue and with involved bilateral neck lymph nodes. In the right neck there was a subdigastric lymph node measuring 2.5×3 cm. and also a lymph node in the jugular chain which measured 1×1.5 cm. There were 2 jugular lymph nodes in the left neck, the largest measuring 2×2 cm. at the level of the hyoid bone.

From July 20, 1970 to September 22, 1970 at the rate of 850 rads per week, 6,000 rads were given to the midline of the base of the tongue and upper necks with parallel opposing Co^{60} fields. At 4,500 rads tumor dose the fields were moved forward to exclude the spinal cord. An additional 1,000 rads tumor dose was given to the primary lesion with a left lateral 18 mev. photon beam. The right lower neck received 5,500 rads given dose and the left lower neck received 6,000 rads given dose with an anterior Co^{60} field. In the second treatment week, because the right subdigastric lymph node was increasing in size, the 12 mev. electron beam was used to treat a 4×6 cm. field-within-a-field, 250 rads twice each week, to 2,000 rads given dose. When the Co^{60} portals were moved off the spinal cord, at 4,500 rads tumor dose, 9 mev. electron beam posterior strips were used to treat both spinal accessory chains to 5,500 rads at 1 cm. depth. The 2 palpable jugular lymph nodes in the left neck received 6 mev. electron beam boosts of 800 rads given dose through 3 cm. circular and 3×4 cm. fields.

At the completion of treatment, the disease in the base of the tongue and in the necks had disappeared. The patient showed no evidence of disease in April 1972.

(*A*) In the upper right neck field a circle about 4 cm. in diameter outlines the growing cervical lymph node. An appositional 12 mev. electron beam field was used to treat it twice a week. (*B*) This is the left neck in the last week of treatment. The upper field covering the angle of the mandible is the boost photon beam field for the primary. The circle in the midneck and the small rectangles in the lower neck are the boost 6 mev. electron beam fields for the cervical lymph nodes. (Reproduced from: Fletcher, G. H., *Textbook of Radiotherapy*.[4])

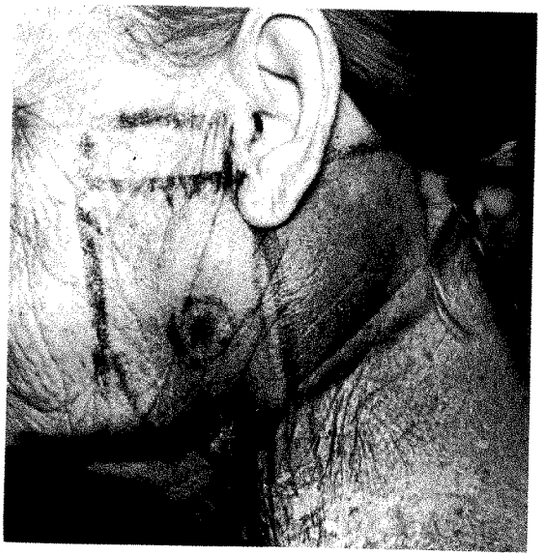


FIG. 9. This 57 year old female was seen in February 1971 with squamous cell carcinoma, Grade III, of the left tonsillar fossa. With a large fixed lymph node at the angle of the jaw, measuring 7×6 cm. and several other smaller, questionably positive lymph nodes along the jugular chain, the staging was T_2N_{3A}.

From February 9, 1971 to April 2, 1971, with parallel opposed Co^{60} fields, the patient received a midline dose of 6,500 rads given at the rate of 850 rads tumor dose per week. The large left lateral portal received a given dose of 5,000 rads. The lower necks were treated with a split field, 5,000 rads given dose in 5 weeks to the right neck and 6,000 rads to the left neck. An additional 1,150 rads with the 22 mev. photon beam were given to the primary through a reduced field. The total tumor dose to the tonsillar fossa lesion (4 cm. depth) was 7,500 rads in 8½ weeks. It had been decided in consultation with the head and neck surgeon that the subdigastric lymph node would loosen enough for a partial neck dissection if a minimum tumor dose of 6,000 rads was given to the whole lymph node. The posterior aspect of the fixed lymph node received an additional 1,750 rads with the 15 mev. electron beam. The right posterior neck received 2,475 rads given dose with the 6 mev. electron beam to bring the dose at 1 cm. depth to 5,100 rads.

On May 3, 1971, the patient had resection of the residual tumor mass in the left neck, and a superficial parotidectomy. A modified left upper neck dissection was done. The mass extended along the internal jugular vein into the retropharyngeal space up to the base of the skull, and to the deep lobe of the parotid. The recovery was essentially unremarkable. The bulk of the mass was completely acellular, with a few scattered islands of recognizable neoplastic squamous cells. There was hyperplastic disorganization sufficient to suggest that the cells were no longer viable. The patient showed no evidence of disease in January 1972.

The patient is shown toward the end of the course of therapy with the boost electron beam field placed over the posterior aspect of the bulging upper neck lymph node. (Reproduced from Fletcher, G. H., *Textbook of Radiotherapy*.[4])

lel opposing fields with a 1:1 loading, the fields are extended back over the chains until the midline tumor dose reaches 4,500 rads. To exclude the spinal cord from further irradiation, the primary fields are moved forward and the 6 or 9 mev. electron beam is used to treat the posterior strips, the dose at 1 cm. depth to at least 5,000 rads (Fig. 5). When parallel opposing fields with a 2:1 loading are being used to treat the primary lesion, a posterior strip on the contralateral side may be treated entirely by the 9 mev. electron beam and by the exit dose of the ipsilateral field which extends back over the spinal cord.

IRRADIATION OF SCAR EXTENSIONS

Posterior extensions of scars can be covered by electron beam strips concomitant with photon beam treatment or as a boost when Co^{60} fields are moved forward off the spinal cord (Fig. 6). Usually 6 mev. electrons can be used. The given dose is 5,000 rads in 4 weeks, if this is to be the only treatment to the scar extensions.

BOOST

After the areas of the primary and both necks have received 5,000 rads with Co^{60}, the electron beam is used at varying energies to increase the dose to the involved lymph nodes in the neck or to areas of high risk of infestation without increasing the dose significantly to the deeper structures such as the pharynx, larynx, or spinal cord. The additional dosage may be 1,000 to 2,500 rads given dose in 4 to 10 treatments through a field limited to the area of re-

sidual lymphadenopathy or induration (Fig. 7). The electron beam is also used to treat a field-within-a-field, if a lymph node continues to enlarge under treatment (Fig. 8, *A* and *B*). The electron beam field is carefully limited to the palpable mass, giving 250 rads twice a week using 9 or 12 mev. to a total dose of 1,500 to 2,000 rads. The concomitant additional treatment replaces the boost usually given at the end of treatment. An electron beam boost may be given to areas of extensive lymph node involvement and a partial or radical neck dissection planned (Fig. 9).

SUMMARY

The electron beam, with energies of 6 to 12 mev., is useful for irradiation of portions of the neck or of the whole neck for a wide variety of clinical situations.

In many of these situations it provides an easy and elegant way to deliver irradiation with minimal dosage to the deeper structures.

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LONG TIME STUDIES OF ADVANCED CANCER OF THE EAR TREATED WITH ELECTROSURGERY PLUS RADIATION*

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IN 1948, 24 years ago, we presented a paper[1] before the American Radium Society dealing with the treatment of advanced cancer of the ear. Thirty-five patients were selected as suitable for study and 18 (51.4 per cent) remained well for 3 to 7 years. The patients selected were treated from 1939 to 1947, at which time we were using combinations of electrosurgery and low intensity radium needle implants, or an orthovoltage series of x-ray treatments given daily except Sunday, until a total of 3,600 r (air) was administered in 13 days.

In this paper we are presenting evidence supporting our present belief that the removal of the invaded portion of the ear with electrosurgery plus the implantation of low intensity radium needles in a layer beneath all of the original tumor for a period of 7 days, delivering point doses varying from 6,000 to 12,000 gamma r, produces the best results[2] except in the rare cases in which the carcinoma has invaded the mastoid and the surrounding bone. When this occurs the entire invaded area first receives the series of x-ray treatments described above, using a primary filter increased through the years from 0.5 mm. of copper to 0.4 mm. of tin and voltages increased from 200 kv. to 260 kv.

At the end of 6 weeks the patient is much improved but the bone structures are still involved and the remaining malignant tumor is carefully destroyed with electrocoagulation, using a general anesthetic. Following this procedure most of the dead tissue is cut away with curved scissors and suspicious areas in the bone are again coagulated. Daily boric acid ointment dressings are started and the patient is discharged.

The dead tissue slowly sloughs away leaving a white scar and the patient returns at intervals for the removal of plaques of dead bone, if they are still present. Complete healing requires from 6 to 8 months. The progress of such a patient treated 23 years ago is shown in Figure 1, *A–F*.

The cases reported in our first article in 1948 all had biopsies indicating that the ear tumors were basal cell or squamous cell carcinomas or combinations thereof. The cure rates were somewhat misleading in that 18 (51.4 per cent) picked from a selected group of 35 were alive with no visible evidence of cancer at 3 to 7 years, but not necessarily well.

The selection of a survival time that indicates a true cure now poses a difficult problem. Certainly a 5 year survival no longer can be accepted as a positive cure, although many such cases remained cancer-free during their lifetimes. After studying our material carefully we decided to accept 12 year survivals without recurrences as cures in our new group of 39 patients with positive biopsies properly treated from 1947 to 1958.

Table 1 lists 14 of these patients living and well for 12 or more years after treatment with no evidence of cancer of the ear. Two of them dying at 12 and 15 years may possibly not have died of cancer of the ear, but they are excluded so that a cure-rate of 12 (85 per cent) is accepted as correct for those followed for 12 or more years, or 30.7 per cent of the entire group of 39 favorable cases treated.

The outcomes of the remaining 25 patients followed from 1 to 10 years and

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3-6, 1972.

thought to have a good prognosis, are tabulated in Table II. Many of these people were old and 14 of them died of intercurrent diseases with no evidence of cancer of the ear from 1 to 7 years after treatment. Another man who obtained an excellent result (Fig. 4, *A–D*) was killed in an automobile accident at 6 years, and 7 patients obtaining good results were completely lost to follow-up. This does not mean that they are necessarily dead because many patients coming long distances from small towns do not return or answer letters so long as they believe that they are well. This leaves only 3 known failures dead of recurrent cancer of the ear at 10, 5 and 3 years after treatment. Although we feel fairly certain that our actual cure-rate should be placed somewhere near 80 per cent, we have no way of establishing this figure mathematically and must allow it to stand at 30.7 per cent, if we accept only 12 year survivals as cures.

Thus far we have omitted the 23 cases listed in Table III treated from 1940 to 1958 and considered incurable at the time of admission. None of them was cured and they are not included in the statistical material used thus far. Sixteen of these patients had received large doses of irradiation before being admitted to our clinic and all experienced radiotherapists know that the addition of more radiation to an area in which radiation fibrosis and infection and cartilage necrosis has been produced may worsen the complications without destroying the malignant tissue. When the damage is not too extensive radical surgery or electrocoagulation done thoroughly offers some hope of success but none of our 23 cases was cured and their only hope lay in the early adoption of an efficient irradiation technique combined with some type of radical surgery (electrosurgery in our Clinic) as the first treatment administered.

Table I

14 PATIENTS WITH ADVANCED CANCER OF EAR TREATED SUCCESSFULLY WITH ELECTROSURGERY, LOW INTENSITY RADIUM NEEDLES AND ORTHOVOLTAGE

(1947 to 1958)

4	patients living and well 25, 23, 22, and 14 years
1	patient lost at 16 years with no cancer of ear
7	patients dead of intercurrent diseases at 20, 15, 15, 14, 13, 13 and 12 years
1	patient died of cancer of the skull at 15 years
1	patient died of pulmonary metastases of unknown origin at 12 years

Twelve cases well 12 to 25 years.
Cure rate 85 per cent.

Table II

25 CASES WITH ADVANCED CANCER OF EAR TREATED NOT KNOWN TO BE WELL 12 OR MORE YEARS

(1947 to 1958)

15	cases with cancer of ear well—died of intercurrent diseases 3 at 7 years, 3 at 6 years, 1 at 4 years, 2 at 3 years, 4 at 2 years, 1 at 1 year and 1 auto wreck at 6 years
3	cases died of recurrent cancer at 10 years, 5 years, and 3 years
7	cases good primary results—lost to follow-up

Good primary results in 22 of 25 = 85 per cent.

REPORT OF CASES

Case 1. M.P. (Age 50 years.) In 1944 a tumor was observed growing in the external auditory canal of the left ear. Two otologists practicing in Chicago were consulted. Neither of them considered the condition serious and simple local treatment was prescribed with no beneficial effect.

When the tumor extended through the external meatus to involve the skin, 2 dermatologists were consulted. One advised injections of cod liver oil, while the other administered

Table III

23 CASES WITH ADVANCED CANCER OF EAR UNSUCCESSFULLY TREATED

(1940 to 1958)

Much irradiation elsewhere before admission	16 cases
Treated with orthovoltage alone	2 cases
Over irradiation	2 cases
Inadequate treatment	1 case
Unsuccessful radical surgery	1 case
Pulmonary metastases of unknown origin	1 case

Not cured, 23 of 23 patients.

Grenz ray treatments for 8 weeks, neither of which was beneficial.

Next he consulted a Chinese doctor who treated him for a swelling over the left mastoid which revealed squamous cell carcinoma, Grade 1. During the next 6 months a series of "serum" injections was given, while the tumor continued to grow.

In 1948 he went to the Sloan-Kettering Institute in New York where 2 surgeons, whose names are unfamiliar to us, advised radical surgery. He was not satisfied with what he was told and returned to Chicago and went to the Michael Reese Hospital, where he was referred to the Department of Radiology.

The radiotherapist advised a series of x-ray treatments, but would not promise him a cure. The tumor was growing rapidly in all directions in the skin surrounding the ear and in June, 1948, he was admitted to the Holy Cross Hospital where he received a course of "chemotrypsin" treatments, without improvement. Pain became severe and the partially necrotic auricle of the ear was removed by a surgeon.

The patient's wife then learned that a Chicago Tumor Clinic had been set up under the directorship of Dr. Max Cutler, whom we had met at the Memorial Hospital in New York. Before taking him there she visited the hospital library and asked to be allowed to see the latest article dealing with the treatment of cancer of the ear included in the medical literature. It so happened that she was shown our well illustrated article titled "The Treatment of Advanced Cancer of the Ear" published in December, 1948. She immediately called us by telephone and asked us to see her husband. At our suggestion she had Dr. Cutler see him and was advised against bringing him to Dallas. However, they appeared in our waiting room the next morning.

At admission on April 24, 1949 he did not look well because of a mental depression, lack of food and heavy sedation. A large oval mass of growing tumor with elevated edges was centered over the original location of the ear and measured about 15.0 cm. in its longest diameter (Fig. 1). A left facial paralysis caused a downward rotation of the lower lip. Roentgenograms showed a complete destruction of the left mastoid and the outer surface, and part of the inner surface, of the skull just below the middle ear. When the gauze dressing was changed it was soaked with purulent fluid.

Beginning on April 25, 1949 he received a daily dose of 300 r (air) until a total of 12 doses (3,600 r) was given to a 15×15 cm. port, including all of the tumor, in 13 days. The treatment factors were 200 kv., a filter of 0.5 mm. Cu and 1.0 mm. Al, and a target skin distance of 50 cm. At 3 weeks his pain was relieved and he could open his mouth one-half inch, which he could not do at admission, apparently because of invasion of the temporomandibular joint.

At 6 weeks the tumor had shown marked regression, particularly about its outer elevated edges, but patches of necrosis and tumor tissue could be seen in the midportion of the lesion indicating that active tumor was still present.

He was then given a general anesthetic and a careful electrocoagulation was done in an effort to destroy all of the abnormal tissue. The active electrode was a heavy darning needle clamped in an insulated handle and it was inserted into points located about 1 cm. apart in the abnormal tissue. At each insertion the current was turned on with a foot switch until the surrounding tissue assumed a grayish color, and in most locations the needle was inserted until it reached bone. All of the coagulated tissue was then cut away with a pair of sharp, curved scissors and residual suspicious tissue was again destroyed. Bleeding vessels were touched with the coagulation needle and partially destroyed fragments of bone were removed with rongeur forceps.

On the following day he felt well and was allowed to return to Chicago where his wife was to apply boric acid ointment dressings daily. He agreed to return in 6 weeks for a check-up examination, but we only received a letter stating that he was well.

This state of affairs continued until 1 year and 4 months after his first visit, when he returned because of discharge and pain in the center of the healed wound where fluid was seen coming from the edge of a plaque of partially burned bone. He was referred to a good surgeon who removed the infected plaque along with others. No cancer was found and he was discharged.

After much persuasion he visited us again 7 years after his first visit. The wound was smoothly healed except for a tiny opening in the upper portion from which a clear discharge soiled the dressing each day. He was able to eat without difficulty and the deformity of the lower lip was much improved. At the end of 17 years we induced him to visit us again at which time the small opening in the scar was

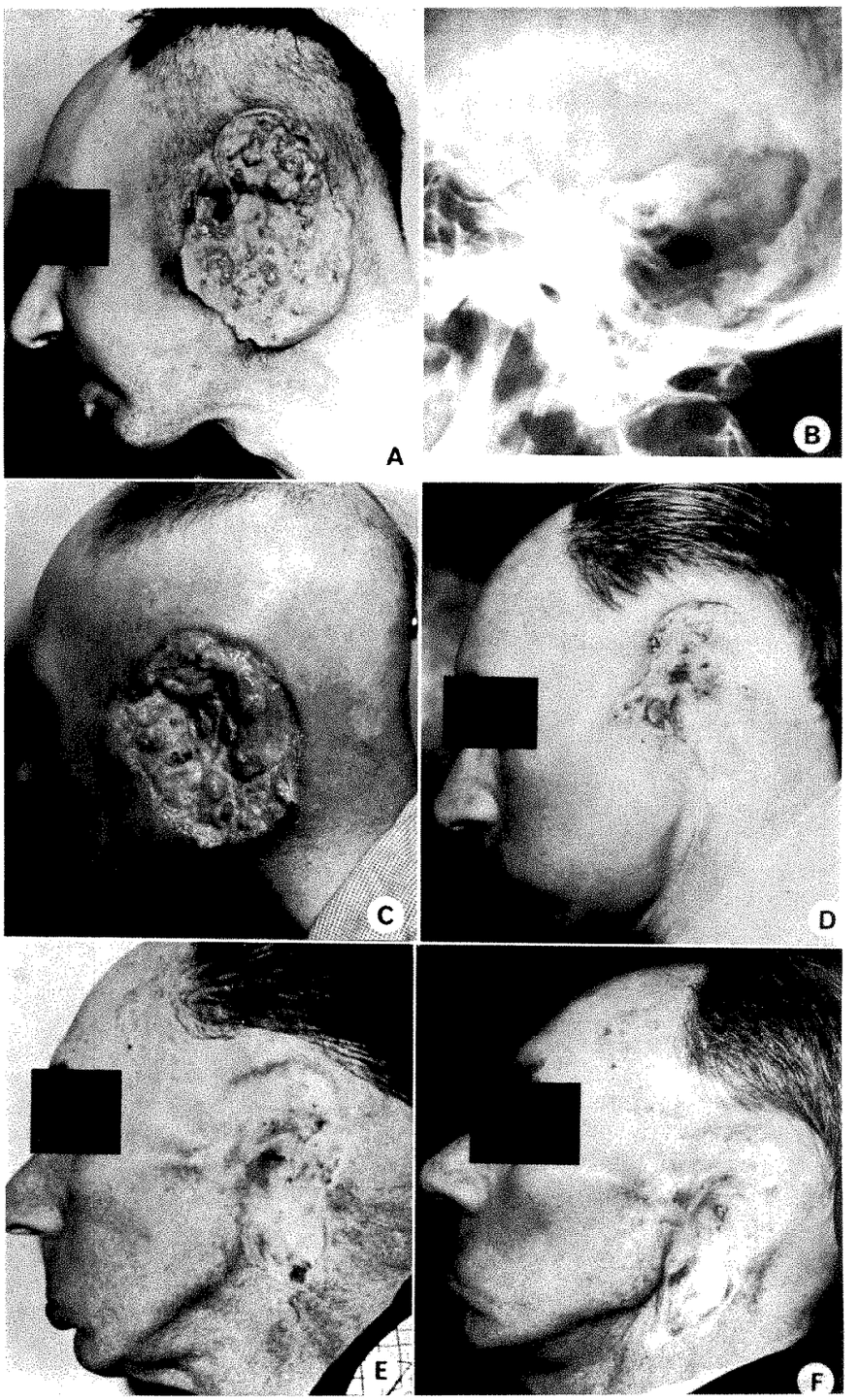


FIG. 1. (*A–F*) *A* and *B* show the large squamous cell cancer growing about the original site of the ear and the destruction of the mastoid and part of the lateral skull in the roentgenogram made at admission; *C*, improvement with slough and active tumor 6 weeks after administration of 3,600 r with orthovoltage; *D*, *E* and *F* show scar observed 14 months, 7 years and 17 years after thorough electrocoagulation of residual tumor. Cancer of ear well at 23 years. Died 4 months later in Chicago of rapidly developing cancer of colon.

still present but the position of the lower lip was much improved.

In April, 1972, 23 years after his first treatment he stated that he felt well at the age of 73 and worked every day in his business just as he did before he was disabled by the cancer of the left ear. He wore a gauze flat over the scar in the treated area and was no longer concerned about the appearance of the scar.

In July his wife called by telephone and stated that he was acutely ill in the Michael Reese Hospital and asked for suggestions relative to his care. She was asked to have his doctor send us a review of his symptoms and the diagnosis. This seemed so reasonable that we did not get the doctor's name. However, the doctor did not communicate with us and a letter from his wife, received on September 3rd, indicated that the patient died in the hospital on August 31st. Two more letters to her have remained unanswered. His rapid downhill course suggests that he did not die from recurrent cancer of the ear.

After writing many letters and enlisting the aid of one of our good radiological friends in Chicago, we finally received a note from the Chairman of the Department of Radiology at the Michael Reese Hospital indicating that the patient died of a cancer of the colon with generalized carcinomatosis and obstructive uropathy. No evidence of cancer of the ear was found and the scar in the left neck produced by our treatment was thought to have been produced by a radical block dissection.

CASE II. G.E.B. (Age 50 years.) A nodule appeared in the left lower ear about 9 months before admission. It grew rapidly after the application of a cancer plaster and involved the entire ear throughout its attachment to the surrounding skin both in front of and behind the structure. There was an ulcerated extension out into the left cheek. A biopsy was reported as epidermoid carcinoma, squamous cell type, Grade I. The facial nerve was not involved and no cervical lymph nodes could be felt. The tumor appeared to extend through the attachment of the auricle to the skull.

The entire ear was removed with an electrosurgical needle which was kept as close to the skull as possible and six 2.4 mg. and two 1.33 mg. radium needles were placed vertically in the upper postoperative wound, and two 2.4 mg. and one 1.33 mg. needles transversely in lower portion for a period of seven days (Fig. 2).

When the patient returned at 6 weeks, all evidence of the cancer was gone and the wound was healed except for a small area in the center of the treated region.

At 9 months, the wound was smoothly healed and he had no evidence of cancer, hearing difficulties or metastatic lymph nodes.

At 3 years, the wound was smoothly healed and he came in to inquire about the construction of an artificial ear.

A letter received in 1971 revealed that he was still alive with no evidence of cancer at 24 years.

CASE III. Mrs. J.C.W. (Age 72 years.) She had first noticed a painless swelling in front of the lower left ear $1\frac{1}{2}$ years before admission and had received 18 x-ray treatments in another city but when she entered our institution a growing tumor measuring 6×7 cm. surrounded and invaded the lower two-thirds of the auricle. Biopsy material was diagnosed as epidermoid carcinoma, squamous cell type, Grade III.

On May 30, 1970 the involved portion of the ear was removed by electrosurgery and the underlying portion was removed with curved scissors. Five 2.4 mg. radium needles were inserted vertically under the tumor bed in the left cheek in front of the ear and four 1.33 mg. needles were placed transversely under the site of the tumor, in and behind the ear. Three 2.4 mg. and two 1.33 mg. needles were then placed transversely under the induration below the ear and the entire pattern remained in place for 7 days (Fig. 3). Although no metastatic lymph nodes were palpable, 7×300 r (air) orthovoltage was given to a portal measuring 7 cm. in diameter directed at the tumor in front of the ear, while the needles were in place.

Six weeks after her therapy all evidence of the cancer was gone and the treated area was covered by a layer of grayish tissue.

She could not return because of a broken ankle, but an infection in the left ear was treated at home several times with penicillin.

At 8 years she returned because of a necrotic area seen overlying the left mastoid. After treatment by a good surgeon this area healed.

She died at home, 13 years after she was treated, when she was 85 years of age and her home physician states that no evidence of cancer of the ear could be found. The cause of death was noted as a cerebrovascular accident.

CASE IV. C.C.P. (Age 64 years.) About 2 years before admission a tumor appeared in



FIG. 2. (*A* and *B*) Squamous cell cancer involving entire ear treated by removal of ear and tumor with electrosurgery and implantation of low intensity radium needles in the base of the tumor for 7 days; (*C*) after the removal of needles; and (*D*) 9 months later, when healing was complete. This patient is alive and well at the end of 24 years.

front of the lower portion of the left ear. It grew steadily until it formed a cauliflower mass measuring 8 cm. in diameter which extended into the attachment of the entire auricle. The biopsy report was squamous cell carcinoma, Grade II, and no metastatic lymph nodes were felt in the neck.

On September 7, 1944 the tumor and the entire ear were removed with the electrosurgical unit and seven 2.4 mg. radium needles were in-



FIG. 3. (*A–D*) *B* and *C* show the infiltrating squamous cell carcinoma invading the lower two-thirds of the auricle; *A*, drawing of the tumor bed after the resection of the lower two-thirds of the auricle and the insertion of low intensity radium needles for 7 days; *D*, healing of the treated area after 6 weeks. She died of a cerebrovascular accident 13 years after treatment with no evidence of cancer of the ear.

serted vertically and five 2.4 mg. and six 1.33 mg. needles transversely in the operated area for a period of 7 days (Fig. 4). At 7 weeks no evidence of cancer could be made out and the operative wound was healing slowly. At 2 years it was smoothly healed about the external auditory canal. The wound was still healed when he was killed in an automobile accident 6 years after his treatment.

CASE V. D.L.S. (Age 58 years.) An ulcerated tumor had appeared surrounding the lower lobe of the left ear and had grown steadily until at admission an irregular ulcer measuring about 8 cm. in diameter had destroyed the lower half of the auricle. A biopsy was reported as squamous cell carcinoma, Grade IV. No metastatic lymph nodes could be felt in the neck (Fig. 5).

The remaining portion of the lower ear was removed with curved scissors after the entire tumor had been destroyed by electrocoagulation, and twelve 2.4 mg. radium needles were inserted in the remaining tissue for a period of 7 days.

At 6 weeks all evidence of the malignant tumor was gone and granulation tissue was appearing in the treated area. The wound was completely healed at 9 months and scar tissue had replaced the site of the coagulation. At 12 years the scar was still smoothly healed when he died at home of some unknown cause.



FIG. 4. (*A–D*) *A*, large squamous cell carcinoma of the left cheek invading the attachment of the auricle to the skull; *B*, low intensity radium needle implantation done after the removal of the tumor with the electric needle; *C*, healing about 6 weeks after removal of radium needles; *D*, ear completely healed at 9 months. This man was completely well when he was killed at 6 years in an automobile accident.

CASE VI. T.F.W. (Age 63 years.) At his first visit on October 18, 1946 this man had the type of skin known to form cancer rapidly. He had malignant tumors on both sides of the upper lip, the left lower lip and the left cheek. The lesions on the upper lip were treated with low voltage roentgen rays and low intensity radium needles were inserted beneath the deeper tumors on the left lower lip and left cheek for 7 days. At 3 months all of the lesions were healed except for a small ulcer in the edge of the treated lesion in the left lower lip. He was asked to return every 6 weeks, so that new lesions could be treated when they were small. He ignored this advice and returned on July 12, 1949 with the large carcinomas involving both ears as shown in Figure 6. The large deep-seated tumor surrounding the lower right ear measured 10.0 cm.

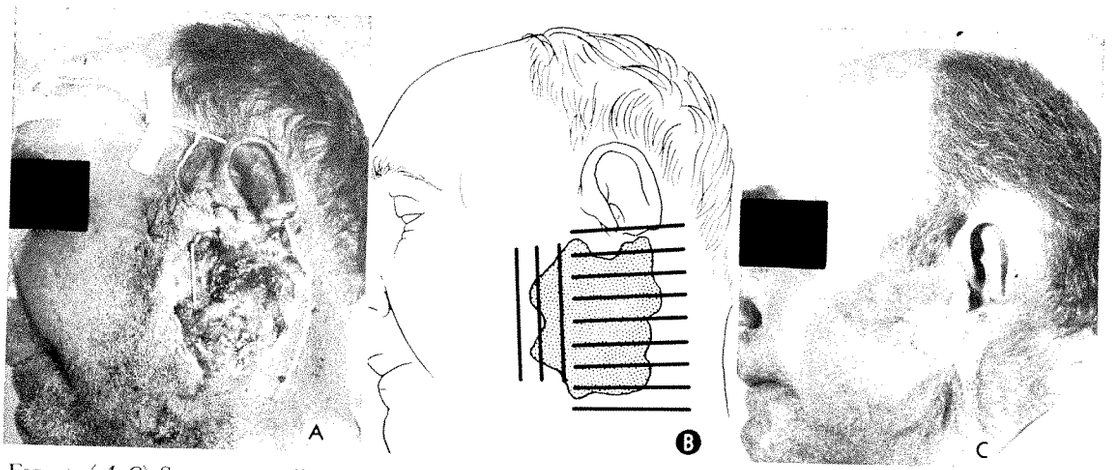


FIG. 5. (*A–C*) Squamous cell carcinoma of lower half of left auricle shown (*A*) following electrosurgery, (*B*) with radium needles in place and (*C*) complete healing at 9 months. He died at home of some unknown cause at 12 years with no cancer of the ear present.

in diameter and extended into the upper neck and the biopsy report was epidermoid carcinoma, squamous cell type, Grade III. The oval tumor seen in front of the left ear measured 3.5 cm. in its longest diameter and the biopsy report was basal cell carcinoma, tricho-epithelioma type. The lower two-thirds of the right ear was removed by electrosurgery and ten 2.4 mg. and seven 1.33 mg. radium needles were inserted in a layer designed to deliver a cancerocidal dose to the large tumor base in 7 days and the tumor in front of the left ear was destroyed by electrocoagulation. While he was in the hospital sizable cancers of the skin of the right temple, the left upper lip and 2 areas on the right neck were treated with low voltage roentgen rays.

Photographs of the face made 3 months later showed complete disappearance of the tumor in front of the left ear and of the malignant tissue which surrounded the right ear (Fig. 6). There was still some granulation tissue present in the wound below the remaining fragment of the right ear, which was healing slowly. He was a good example of what we often refer to as a "Chronic Cancer Haver" because he had something in his body which continued to produce new malignant tumors on skin surfaces exposed to sunlight. He was warned of the importance of having new lesions treated as they appeared, but we did not see him again and learned through a visiting nurse that he was using a face mask and an ointment given to him by a cancer charlatan. He died on January 28, 1953 of metastatic cancer some 7 years after he first entered our Clinic.

SUMMARY

This paper follows our first report on the same subject presented before the American Radium Society 24 years ago, in 1948.

Records of 62 cases treated from 1940 to 1958 were collected and divided into 3 groups.

The first group of 14 cases includes proven cures alive from 12 to 25 years (Table 1). Two were excluded because 1 died of cancer of the skull near the original ear lesion at 15 years and 1 died of pulmonary metastases at 12 years with no evidence of cancer of the ear present. This leaves 12, or 85 per cent, of the original 14 cases well from 12 to 25 years. All of these, except 1, were treated by the removal of the original lesion with electrosurgery plus the implantation of low intensity radium needles beneath the remaining malignant tissue for 7 days. The 1 exceptional case had a large squamous cell carcinoma surrounding the original site of the ear plus extension into the mastoid and bone surrounding the internal ear. Treatment was started with 3,600 r (air) given through a large port to the entire lesion in a period of 13 days using orthovoltage. Six weeks later the tumor showed marked improvement, but the remaining portion was then destroyed by careful electrocoagulation of the mastoid and residual involved bone be-

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SIGNIFICANCE AND TREATMENT OF LYMPH NODE METASTASES OF MALIGNANT MUCOUS AND SALIVARY GLAND TUMORS*

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LYMPH NODE metastases of mucous and salivary gland tumors were thought at some time to be rather rare. This was especially so in the thirties and early forties when almost all these tumors were called mixed tumors.[1] Parotid tumors which are by far the commonest of the whole group were particularly vulnerable to this mistake. It was only in the early fifties when the different types of mucous and salivary gland tumors became well defined that the natural history (and lymph node metastases) started to be appreciated. It is now recognized that lymph node metastases occur in about one quarter of all the malignant tumors of the various mucous and salivary glands.[3,4,6]

MATERIAL AND METHOD

Forty-three patients with lymph node metastases of mucous and salivary gland origin are discussed in this series (Table 1). These were found in a group of 179 cases reported by the author in another publication.[5]

The parotid gland is the commonest site of origin of the primary tumor followed by the palate and submandibular gland in close succession. While the lymphatic drainage of the mucous glands of the upper air and food passages is the same as that of the mucous membrane itself, that of the major salivary glands is somewhat different and worth discussing in some detail.

LYMPHATIC DRAINAGE OF PAROTID GLAND (Fig. 1)

Most of the lymphatics of the parotid gland drain into the parotid lymph nodes which are divided into 3 groups:

1. Superficial preauricular lymph nodes situated anterior to the tragus and superficial to the deep fascial capsule of the parotid gland.

2. Subfascial lymph nodes, which are found deep to the deep fascial covering of the parotid. Two subgroups are identified: the deep preauricular lymph nodes situated either in an antetragal position, or somewhat more anteriorly; and the subauricular lymph nodes situated between the posterior aspect of the parotid gland and the sternomastoid muscle.

3. Deep intraglandular lymph nodes, which are found mainly in the so-called isthmus of the gland. They are usually grouped along the external jugular and the posterior communicating facial veins and

TABLE I

INCIDENCE OF LYMPH NODE METASTASES IN MALIGNANT SALIVARY AND MUCOUS GLAND TUMORS

Site	No. of Cases with Malignant Tumors	No. of Cases with Lymph Node Metastases
Parotid gland	66	16
Submandibular and sublingual glands	21	8
Oral cavity	31	9
Upper air passages*	40	4
Larynx and trachea	8	1
Pharynx	6	4
Esophagus	1	—
Lacrimal gland	6	1
Totals	179	43

* Including nasopharynx.

* Presented at the Fifty-fourth Annual Meeting of the American Radium Society, in Joint Session with the James Ewing Society, and the Society of Head and Neck Surgeons, Boca Raton, Florida, May 14–19, 1972.

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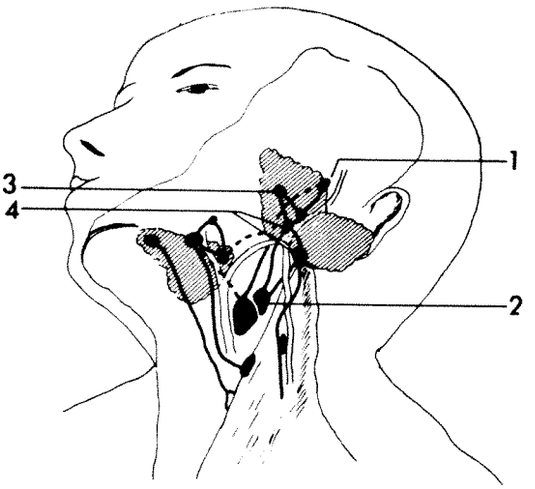


Fig. 1. Lymphatic drainage of the parotid and submandibular glands: 1. superficial preauricular lymph node; 2. jugulo-digastric lymph node; 3. deep preauricular lymph node; 4. deep intraglandular lymph nodes.

(Redrawn from Rouvière, H.: Anatomie des Lymphatiques de l'Homme, Masson et Cie, Paris, 1932.)

rarely along the external carotid artery, which lies deep in the gland.

However, most of the lymphatics from the parotid gland drain in the second and third groups. The efferent lymphatics from the 3 groups usually terminate in the upper cervical and jugulo-digastric lymph nodes. On rare occasions, a lymphatic trunk drains directly into the submandibular lymph nodes and consequently into the middle cervical lymph nodes. Therefore the lymphatic spread of a malignant parotid lesion most commonly affects the jugulo-digastric and upper deep cervical lymph nodes (*vide infra*), but may on rare occasions involve primarily the middle deep cervical lymph nodes.

Lymph Drainage of Submandibular Gland

Lymph drainage of submandibular gland was discussed in another publication by the author[8] and is summarized as follows:

1. Lymph vessels which end in the submandibular lymph nodes and drain mainly the surface and lateral aspects of the submandibular salivary gland.

2. Lymphatics which drain directly into the deep cervical lymph nodes. This route is more constant than the first one and usually drains the deep portion of the gland. These vessels usually follow the path of the facial artery, ending in the jugulo-digastric and/or upper deep cervical lymph nodes. An occasional lymphatic may reach the middle cervical lymph nodes.

Lymphatic Drainage of Sublingual Gland

Lymphatics draining the sublingual glands have 2 routes, one anterior and the other posterior. The anterior route arises mainly from the anterior part of the gland, traverses the mylohyoid muscle and the area between this muscle and the anterior belly of the digastric ending in the submandibular lymph node situated at the anterior aspect of the submandibular salivary gland. The posterior routes are usually 3 in number, draining the posterior two-thirds or three-quarters of the sublingual gland. Rouvière[9] gave a detailed description of these routes, 2 of which drain into the jugulo-digastric lymph nodes, while the third ends in the middle cervical lymph node which lies between the posterior belly of the digastric and anterior belly of the omohyoid muscles.

Lymphatics draining the 3 major salivary glands end ultimately in the jugulo-digastric and upper deep cervical lymph nodes. An occasional trunk drains into the middle deep cervical lymph nodes. The frequency of lymph node metastases goes hand-in-hand with this pattern.

The jugulo-digastric and upper deep cervical lymph nodes are the commonest groups of lymph nodes involved (Table II). These 2 groups were positive in two-thirds of the cases discussed followed by the submandibular lymph nodes which were involved in about 15 per cent of the cases. Considering the radiation therapy of metastatic lymph nodes from mucous and salivary glands, these 3 groups can be included in one concise treatment volume. This aspect will be discussed later in this study.

As with other malignant tumors of the

upper air and food passages, the incidence of lymph node metastases varies according to the site of origin of the primary. Lesions of the tonsils (2 cases), posterior third of the tongue (7 cases), oropharynx (3 cases), and nasopharynx (5 cases), have the highest incidence of lymph node metastases, 100, 55, 66 and 40 per cent, respectively. This is noticeably higher than in parotid gland tumors (24 per cent). The 2 sites where this mode of spread is least common are the palate (1 of 14) and the paranasal sinuses (2 of 34). These differences are closely linked to the abundance of lymphatics in some sites or their paucity in others.

There is no significant difference in the incidence of lymph node metastases among different types of malignant salivary tumors (Table III) which averages 25 per cent in the 4 most prevalent types: malignant mixed tumors; cylindromas; adenocarcinomas; and anaplastic tumors. However, well-defined mucoepidermoid tumors and acinic cell adenocarcinomas are characterized by their relatively benign behavior and very low incidence of lymph node metastases.[3] On the other hand, lymph node metastases in the poorly-differentiated mucoepidermoid tumors are rather high,[2,10] with an incidence of about one-third of the reported cases. None of the 7 mucoepidermoid tumors in this study metastasized to lymph nodes.

THE SIGNIFICANCE OF LYMPH NODE METASTASES

To discuss the effect of lymph node metastases on the natural history of the disease as well as the results of treatment, it is important to classify the cases or stage them on clinical grounds. Such clinical staging has not evolved internationally yet. In a previous publication, the author proposed the following classification along the lines suggested by the UICC for other malignancies:

- N_0 No palpable lymph nodes
- N_1 Mobile homolateral lymph nodes palpable in the regional draining areas
- N_2 Palpable fixed homolateral lymph nodes
- N_3 Involved contralateral lymph nodes

To try to define a relation between the natural history of the disease and the presence of lymph node metastases is a hazardous course in this study due to the small number of cases. However, a few trends were evident and are summarized as follows: lymph node metastases are far commoner in locally advanced tumors than in early ones. In parotid tumors, for instance, the incidence of lymph node metastases in previously untreated tumors that have involved the skin is 3 times that in similar tumors where the skin is intact. Skin invasion in previously untreated parotid tumors is a recognized sign of locally advanced

Table II

SITES OF OCCURRENCE OF LYMPH NODE METASTASES

Group of Lymph Nodes Affected	No. of Cases
Jugulo-digastric	15
Upper deep cervical	14
Submandibular	7
Middle deep cervical	4
Spinal accessory	2
Lower deep cervical	2
Preauricular	1

Table III

INCIDENCE OF LYMPH NODE METASTASES

Type of Tumor	Total No. of Cases Studied	No. of Cases with Lymph Node Metastases	Per Cent of Incidence
Malignant mixed tumors	19	5	26
Adenocarcinomas	71	18	26
Cylindromas	54	11	20
Anaplastic tumors	20	5	25
Mucoepidermoid tumors	7	0	0
Squamous cell carcinomas	8	4	50
Total	179	43	24

TABLE IV

GENERAL RESULTS OF TREATMENT

	Total No. of Cases	No. of Cases with Persistent Disease	No. of Cases with Recurrent Disease	No. of Patients Dead with Disease	5 Year Results			Method of Treatment			
					No. of Cases Followed	Alive and Well	Alive with Disease	Surgery	Radiation Therapy	Combined Approach	Undetermined or No Treatment
Malignant mixed tumors	5	2	1	3[a]	5	1	1	2	2	—	1
Adenocarcinomas	18	10	3	15[c]	18	2	1	1	13[b]	3	1
Cylindromas	11	5	—	8[d]	11	3	—	1	5[e]	3[f]	2
Anaplastic tumors	5	4	1	5	5	—	1	—	2	1	2
Squamous cell carcinomas	4	4	—	4	4	—	—	—	1	2	1
Totals	43	25	5	35	43	6	3	4	23	9	7

[a] One patient died postoperatively; [b] in 4 cases the lymph nodes disappeared completely under radiation therapy; [c] 1 patient died postoperatively; [d] 1 patient died postoperatively, 1 more patient eventually died without disease; [e] in 2 cases the lymph nodes were completely controlled; [f] in 1 of these cases the lymph nodes were completely controlled by irradiation only.

disease. This finding holds true for tumors originating in other sites except perhaps for tumors of the nasopharynx, tonsil and posterior third of the tongue where lymph node metastases may occur early or be the presenting picture. In 1 of our patients, the tongue lesion did not demonstrate itself until about 6 months after the patient's presentation for treatment, despite regular repeated examinations of the tongue during this period.

Lymph node metastases were demonstrable at time of presentation in half the cases (21): 12 were staged as N_1; 5 as N_2; and 4 as N_3. The rest developed during the course of the disease. The time lag between presentation and development of lymph node metastases varies among the different histologic types. Cylindroma is characterized by a relatively long natural history and time lag. Two of our patients developed the lymph node disease after more than 5 years, 6 and 8 years to be precise. Malignant mixed tumors and adenocarcinomas are somewhat similar with 3 patients (out of 5) and 4 (out of 18) developing the lymph node metastases late in the course of the disease. However, all the patients with squamous cell carcinoma had demonstrable lymph node disease at presentation. The average time lag in all histologic types is 3 years and 4 months. This is probably related to the long history of these tumors and their rather slow growth pattern.

The great majority of lymph node metastases are demonstrated while the primary lesion is present, whether previously untreated, recurrent or persistent after previous treatment. In only 7 cases (of 42) did the metastatic lymph nodes present while the primary was grossly controlled. Should this finding be valid, a therapist, be he surgeon or radiotherapist, would be more concerned with the control of the primary rather than that of occult lymph nodes except perhaps in certain sites, *e.g.* the tonsils or the posterior third of the tongue. This problem is more critical to the surgeon than the radiotherapist. While the site of origin, the jugulo-digastric and the upper deep cervical lymph nodes (the most common sites of lymph node metastases) usually represent one treatment volume to the radiotherapist, the scope of surgery would have to be markedly increased if both are to be dealt with rather than the primary only.

EFFECT OF LYMPH NODE INVOLVEMENT ON RESULTS OF TREATMENT

This, of course, is the most significant

TABLE V

RESULTS OF TREATMENT OF PREVIOUSLY UNTREATED CASES

Total No. of Cases	No. of Recurrent Tumors	No. of Cases Dead of Disease	No. of Cases with Persistent Disease	No. of Cases Followed up for 5 Years	No. of Cases Alive	
					Free of Disease	With Disease
21	6	15	10	21	5	2

aspect of the presence of lymph node metastases. It is clear from a look at Table IV that the results of treatment are very poor. In over half the cases (25 of 42), there was residual lymph node disease after treatment. However, this was much more significant in recurrent cases than those previously untreated. The incidence of residual disease in the latter was 28 per cent (Table V). Moreover, 80 per cent of the patients died with their disease. The average survival of patients after treatment of the lymph node metastases was 15 months, but 7 patients lived over 2 years and 2 patients lived for over 5 years with their disease. Of the 43 patients who were followed for 5 years, only 6 were alive and well (14 per cent). Again previously untreated patients faired better; the 5 year survival percentage (free of disease) was 28 per cent (5 of 18).

It would be interesting to try to define some relation between the clinical staging of the disease and the results of treatment. The previously untreated cases are the only cases to be staged, recurrent cases are technically excluded.

The 4 patients staged as N_3 continued to have persistent disease, and all died in less than 2 years. All 5 patients staged as N_2 continued to have persistent disease, and all but 1 died in the first year. The fifth patient lived for 5 years with persistent disease. Thus, none of the 9 patients staged N_2 and N_3 were alive and well after 5 years; 8 of them died in the first 2 years.

In the N_1 group 5 patients (of 14) were alive and well. Two of these had tumors of the posterior third of the tongue, 2 had tonsillar tumors, and the fifth had a tumor in the submandibular gland.

Thus, the only patients alive and well after 5 years were those where the lymph nodes were discovered at an early stage (N_1).

Whether the results of treatment of patients who suffered from lymph node metastasis while the primary was under control are different from those where both the primary and lymph nodes were present, is open to speculation. The number of cases is too small to reach any conclusion (Table VI). However, 2 cases were alive with disease after 5 years; 1 was treated with surgery and the other with radiotherapy (Cases I and VI). Two cases were not treated; 1 died after 4 months and the other after 11 months with distant metastases. Lymph node disease was not considered the major problem (Cases III and VII). One case was treated with radiation therapy, but the disease persisted and the

TABLE VI

RESULTS OF TREATMENT OF CASES WITH LYMPH NODE METASTASES ONLY

	Primary Controlled
Case I.	Tumor recurred after 3 years; patient alive with disease after 5 years; treated by surgery
Case II.	Alive and well after 5 years; treated by radiotherapy
Case III.	Continued to have persistent disease and died after 4 months; no treatment given
Case IV.	Continued to have persistent disease and died after 6 months; treated by radiotherapy
Case V.	Died postoperatively; treated by surgery
Case VI.	Disease recurred; alive with disease after 5 years; treated by radiotherapy
Case VII.	No treatment to lymph nodes which continued to be stationary; died after 11 months with distant metastases

TABLE VII

RESULTS OF TREATMENT ACCORDING TO METHOD OF TREATMENT

	Total No. of Cases	No. of Cases with Persistent Disease	No. of Cases with Recurrent Disease	No. of Post-operative Deaths	No. of Dead with Disease	5 Year Results		
						Total No. of Cases	Alive and Well	Alive with Disease
Surgery	4	1	1	2	1	4	—	1
Radiotherapy	23[a]	14	2	—	18	23	4	2
Radiotherapy+Surgery	9[b]	2	2	1	7	9	2	—

[a] In 7 cases the lymph nodes disappeared completely under irradiation; [b] in 1 case the lymph node disease was controlled by radiotherapy.

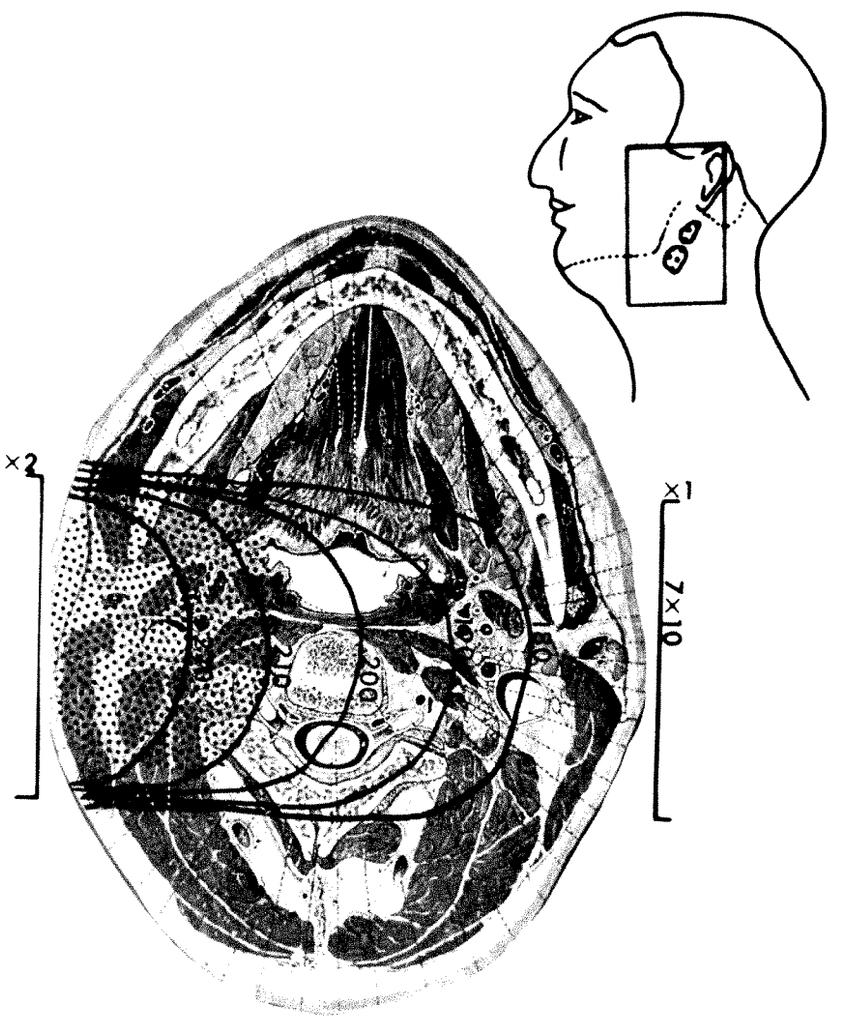


FIG. 2. Plan to treat lymph node metastases with 2 lateral opposing fields on Co^{60} unit.

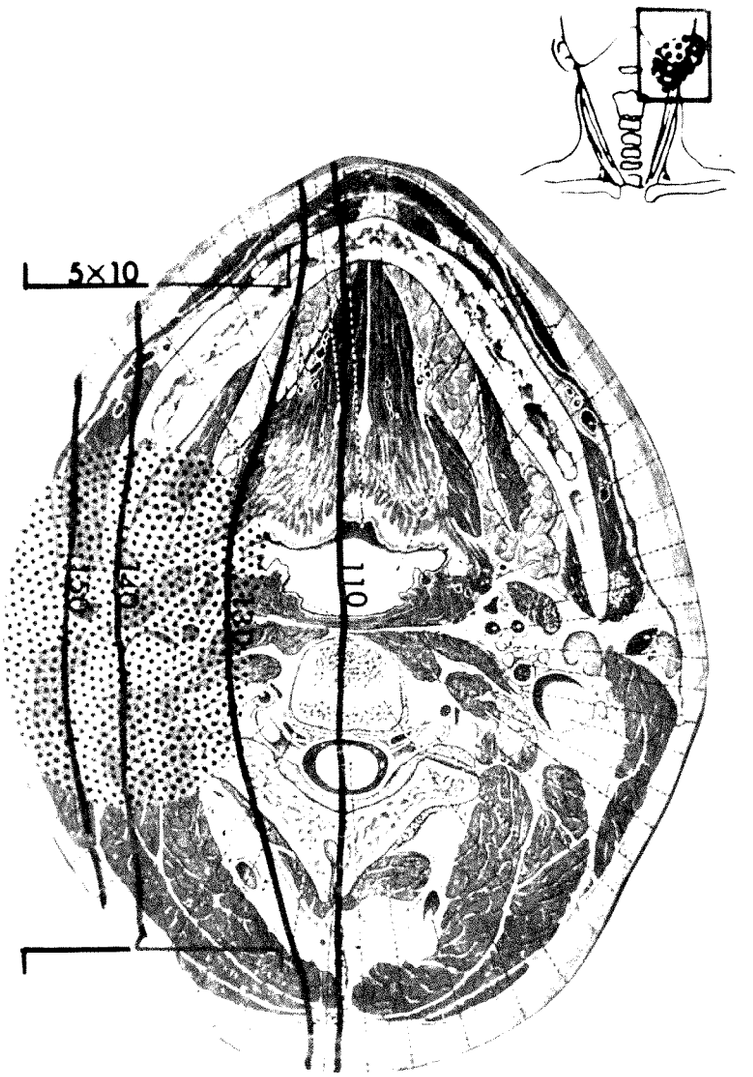


Fig. 3. Plan to treat lymph node metastases with 2 anterior and posterior opposing fields on Co^{60} unit.

patient died after 6 months (Case IV). One patient died postoperatively (Case V). Only 1 patient was alive and well after 5 years (Case II). This patient was treated by radiation therapy alone.

Another question impossible to settle is whether the histologic type of primary tumor has any effect on the results of treatment. The figures in Table IV seem to suggest that patients suffering from lymph node metastases due to cylindroma may do marginally better than those in other categories, but the number of cases is too small to allow this finding any statistical significance.

This series is from a radiotherapy center, where most of the cases are treated either by radiotherapy alone or in combination with other modalities (Table VII). Because of this and of the small number of cases, it is very difficult to reach any conclusions regarding the choice of the method of treatment. Moreover, no comparable series treated by surgery alone have been re-



Fig. 4. Uvex cast for beam direction.

ported. The sporadic results published so far are along the same lines discussed here. A few findings in this study are worthy of note: radiotherapy succeeded in controlling the lymph node diseases in 9 (of 23) cases; there was only 1 subsequent recurrence in the lymph nodes; however, primary disease recurred in 2 more cases; a third group of patients died with distant metastases, while the lymph node region continued to be free of gross disease. While it is granted that a good number of those patients have advanced disease and are beyond cure, there is still a group which may be salvaged by a subsequent operative excision. While complications of such an operation, mostly a radical lymph node dissection, after radiotherapy are somewhat higher than without radiation therapy, these could and should be kept to a minimal degree by judicial application of radiation and careful dissection of the lymph nodes.[8] In applying radiation, the therapist will do well if 2 facts are taken into consideration: lymph node metastases of mucous and salivary gland tumors are most common in jugulo-digastric and upper cervical lymph node areas, rarely does the disease spread wider than these 2 stations; and the dose necessary to achieve complete regression of the lymph node disease is usually around 6,500 rads tumor dose given in about 6 and a half weeks. Giving such a dose to a large volume, *e.g.* the whole cervical lymph node chain, is neither necessary nor advisable in every case especially since this may jeopardize the chances of subsequent successful surgery. A small volume high dose radiation course should be aimed at.

Technique of Radiation Treatment

The plans seen in Figures 2 and 3 are the ones most commonly used to treat the region of the jugulo-digastric and the upper deep cervical lymph nodes. Their disadvantages are obvious: an unduly high dose to the oral cavity and spinal cord (Fig. 2). The relative inhomogeneity and high dose to the skin are other draw-backs (Fig. 3). An electron beam may be employed to deliver a homogeneous dose to the volume irradiated, but the bone shielding effect and the relatively low skin sparing effect of a 15 mev. beam are points to be contended with. The utilization of a cast (Fig. 4) to enable the use of 2 small wedge fields seems to yield a satisfactory plan of treatment (Fig. 5). The treatment volume is kept intentionally large to demonstrate the advantages of this plan. Moreover, such a large volume would be necessary if several lymph nodes are to be included in the volume to be treated. This plan is but an example; the exact size and location of the treatment volume will depend on the particular case treated. The dose to the spinal cord is about half that of the maximum tumor dose (which is delivered to the greatest part of the volume treated). The dose to the oral cavity and pharynx varies from a maximum of 60 per cent of the maximum tumor dose to a minimum of 30 per cent. A dose of 6,500 rads may be delivered to the treated volume in about 6 weeks quite comfortably through this plan. Check-up roentgenograms and direct measurements may be employed to verify the accuracy of the set up.

Conclusions

Of 179 malignant mucous and salivary gland tumors reviewed, 43 (24 per cent) demonstrated lymph node metastases. Tu-

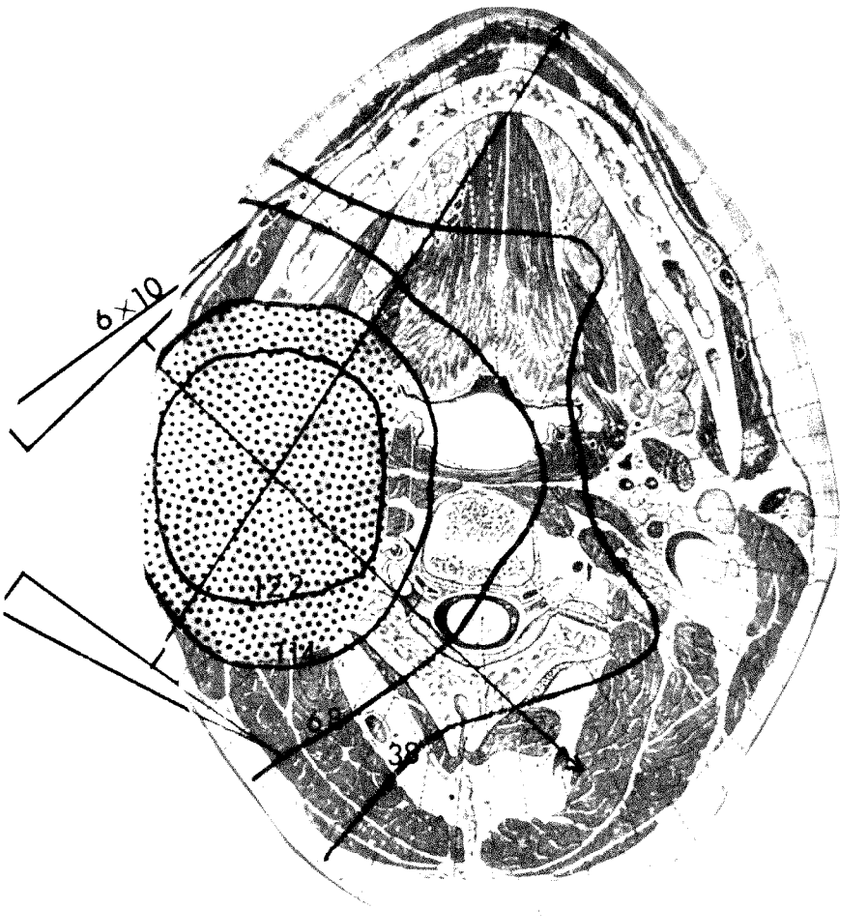


Fig. 5. Plan to treat lymph node metastases with 2 wedge pairs on Co^{60} unit, utilizing the cast seen in Figure 4.

mors in upper air and food passages including pharynx, tongue and buccal mucous membrane have a relatively higher incidence of lymph node involvement; 14 out of 28 cases were affected, while tumors of maxillary antrum and ethmoids disseminate less readily in lymph nodes.

The groups of lymph nodes mostly involved were the jugulo-digastric, upper deep cervical and submandibular in this order of frequency.

The method of treatment in this series was largely a combined approach of excision and radiotherapy. Twenty-two per cent of those treated were alive and well after 5 years.

The effect of the presence of lymph node metastases on the results of treatment, whether in terms of survival or recurrence, is unfavorable. However, when the site of original tumor is the tonsil or the base of tongue, the presence of involved lymph nodes does not affect the prognosis adversely, provided the lymph nodes are mobile. When the contralateral lymph nodes were affected, it was not possible to salvage any case regardless of the site of the original tumor.

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COMPARATIVE ANALYSIS OF TWO REGIMENS OF SPLIT COURSE RADIATION IN CARCINOMA OF THE LUNG*

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CARCINOMA of the lung remains the leading malignancy in terms of incidence and deaths despite recent advances in surgery, radiation therapy, and chemotherapy. There will be an estimated 76,000 new cases of carcinoma of the lung in 1972 with an estimated 69,000 deaths from this disease.[7] It is evident from these figures that only a small percentage of primary carcinomas of the lung are resectable and potentially curable lesions. The vast majority of these patients will go on to die despite the intervention of the surgeon, radiotherapist, or chemotherapist.

The survival of most patients with these unresectable lesions is at best measured in months. A lengthy hospital course to receive treatment for this disease is therefore perhaps both psychologically and financially disastrous.

It has been shown that survival and quality of survival of the inoperable patient are both improved by radiation therapy.[6] Guttman[3] reported a 5 year survival of 7.4 per cent of a selected group of nonresectable patients with the use of radiation therapy alone. Approximately 75 per cent of all the patients treated receive significant palliation of the distressing symptoms of cough, hemoptysis, and pain.[1]

Caldwell and Bagshaw[2] state that survival is improved with higher doses of radiation; but at the same time they recognize the high percentage of patients who exhibit metastases, either during or shortly after a continuous course of radiation. Holsti,[4] Levitt,[5] and Abramson and Cavanaugh[1] have proposed split course techniques for carcinoma of the lung. One advantage of these techniques is to enable the radiotherapist to recognize most of the 20 per cent of patients who will exhibit metastatic disease before completion of a lengthy course of treatment.

MATERIAL AND METHOD

From May 1969 until November 1970 we entered patients into a protocol designed to study 2 different split course regimens. Ninety-seven patients were entered into the study and assigned by a table of random numbers to receive either 3,000 rads in 10 treatments followed by an interval of 1 month with repetition of the same course, or 2,000 rads in 5 treatments followed by the same course after a month's rest. The 2 groups were comparable in age, sex ratio, percentage having had thoracotomy, and those completing the prescribed course (Table 1).

All patients had histologic or cytologic

TABLE I

STATISTICS OF SAMPLE

	A (3,000 rads)	B (2,000 rads)
No.	46	51
Male:Female	40:6	47:4
Thoracotomy	30.4%	41.2%
Average age	61.0	63.2
Did not finish both courses	14	9

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TABLE II

MEAN SURVIVAL
PATIENTS SUBMITTED TO STUDY = 97
(3,000 rads × 2 = 46; 2,000 rads × 2 = 51)

Mean Survival	Days	Months
All patients	231	7.6
3,000 × 2:		
Entire group	259	8.5
Complete therapy (32)	324	10.7
First course only (14)	112	3.7
2,000 × 2:		
Entire group	206	6.8
Complete therapy (42)	229	7.5
First course only (9)	99	3.3

proof plus clinical evidence of carcinoma which was not resectable at the time of thoracotomy or considered inoperable for medical reasons or because of extensive spread of the primary tumor. Thirty-seven per cent of the patients in this study underwent thoracotomy with only biopsy performed. Patients with positive supraclavicular lymph nodes or scalene node biopsy were included in the study as were patients with mediastinal lesions without involvement of the opposite lung, as long as it was possible to encompass the primary tumor and its extensions in a single treatment field with a margin of 1–2 cm.

Cobalt 60 teletherapy or 18.6 mev. photons were used in all cases. Treatment was delivered through anterior and posterior parallel opposing fields with both fields treated daily. The dosage was calculated at the midline, and the differential absorption of lung was not considered.

Epidermoid, undifferentiated, anaplastic, and adenocarcinoma cell types were included in the study. Certain patients were excluded from the study: (1) patients referred for radiation therapy to the mediastinum after resection of the primary tumor; (2) patients with Pancoast tumor; and (3) patients receiving concurrent chemotherapy.

Forty-six patients were randomized into the 3,000 rads group (Group A), and 51 patients were randomized into the 2,000 rads group (Group B). All patients were followed at least 18 months or until death. Two patients were lost to follow-up and were presumed dead at the date of the last scheduled follow-up. Survival time was calculated from the start of radiation therapy.

RESULTS

All patients entered into the study received the first segment of the split-course treatment. Twenty-three patients (24.7 per cent) did not receive the second portion of the course; 15 of these did not return for the second course. Complete treatment was not given to the other 8 patients because of the development of metastatic disease outside the previously treated area during the rest interval.

The mean survival for the entire group of 97 patients was 7.6 months (Table II). The mean survival of those patients who did not complete the prescribed course of radiation therapy was less than half that of the patients who completed both segments of the split course. The mean survival for the patients in Group A was 8.5 months compared to 6.8 months for those in Group B.

The survival at intervals for those patients who completed both courses of therapy is presented in Table III. There is significantly better survival at the 12 month interval for the patients in Group A, according to the chi-square test.

Table IV presents the survival at various intervals following radiation therapy. Nineteen per cent of all patients entered into the study were living at 12 months. The chi-square test showed no difference in survival between Group A and Group B at any time interval following treatment. Only 1 patient survived beyond 24 months without evidence of disease. Two patients in Group A were living at 24 months with evidence of metastatic disease. One patient in Group B is living beyond 24 months and has recently shown evidence of recurrent or persistent disease in the right hilus. The sole survivor with no evidence of disease at

TABLE III

SURVIVAL AT VARIOUS TIME INTERVALS
PATIENTS WHO COMPLETED BOTH COURSES OF THERAPY

Time after Treatment	3,000×2		2,000×2		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total	32		42		74	
3 months	28	88	42	100	70	95
6 months	19	59	22	52	41	55
9 months	13	41	12	29	25	34
12 months	11	34*	5	12	16	22
18 months	7	22	2	5	9	12

* Significant $P<(0.05)$.

this time had a large cell undifferentiated carcinoma, presenting with superior vena cava obstruction.

DISCUSSION

The results presented here for the 2 radiation courses do not show significant improvement over previously reported series, but they are thought to be at least comparable. We believe that the 3,000 rads course may be the more efficacious of the 2 treatment regimens and that the advantages of excluding those patients who exhibit early metastatic disease justifies the use of this type of radiation therapy.

As a referral center for the entire state of Iowa, most of our patients are necessarily hospitalized during their radiation treatment. For this reason we prefer to treat with high intensity split course radiation therapy in this type of malignancy to allow these patients as much time at home as possible.

The over-all survival of 1 per cent at 24 months is somewhat less than what other centers have reported. One must consider, however, that all the patients treated by this method were judged either unresectable at thoracotomy or inoperable according to medical indications. The 24.7 per cent of patients who did not complete both courses corresponds rather well with previous reports of those patients who might develop metastatic disease during a continuous 6,000 rads course. Indeed, this 24.7 per cent of patients would certainly have been overtreated as emphasized by Caldwell and Bagshaw[2] in their paper.

Another advantage of this treatment regimen is that the first half of the split

TABLE IV

SURVIVAL AT VARIOUS TIME INTERVALS

Time after Treatment	3,000×2		2,000×2		Total	
	No.	Per Cent	No.	Per Cent	No.	Per Cent
Total	46		51		97	
3 months	34	74	45	88	79	81
6 months	22	48	23	45	45	46
9 months	14	30	13	25	27	28
12 months	12	26	6	12	18	19
18 months	8	17	2	4	10	10
N.E.D. 24 months	1	2	0		1	

N.E.D. = no evidence of disease.

course was sufficient to afford palliation to these patients. Most of the patients who are dead expired outside this hospital, so no analysis regarding the presence or absence of disease within the treated area could be made.

Although split course therapy appears to have advantages, as reported by Holsti,[4] further work should be done on the dose per fraction and the rest interval. We are attempting to devise further studies to apply to this group of patients.

SUMMARY

Ninety-seven patients were entered into a prospective randomized study of 2 split course regimens of radiation therapy for inoperable carcinoma of the lung.

Group A received a 3,000 rads course with a month's interval followed by a like course; Group B received an initial course of 2,000 rads in 5 treatments followed by a month's rest and repetition of the same course.

The survival of the patients completing both segments of the split course was significantly better in Group A than in Group B at 12 months, but not at 18 months. The over-all survival, free of disease, at 24 months was 1 per cent.

Further studies are needed to achieve a better definition of the time/dose relationships in split course therapy for carcinoma of the lung.

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SUPERIOR VENA CAVAL SYNDROME: SCINTIPHOTOGRAPHIC EVALUATION OF RESPONSE TO RADIATION THERAPY*

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UNILATERAL or bilateral edema of the upper limbs and face, prominent venous engorgement of the neck without concomitant edema of the lower limbs—these symptoms suggest the clinical diagnosis of superior vena caval syndrome. Such symptoms are the result of obstruction of the superior vena cava and its tributaries. In about 80 per cent of the cases the obstruction is thought to be due to malignant intrathoracic neoplasm.[1] In the remaining cases the cause is benign, and in most of these the condition is curable.[3,6,10]

Collateral venous pathways develop wherever there is complete occlusion of the superior vena cava or its tributaries. Prominent venous channels appear over the chest and abdomen after the formation of these collaterals. Collaterals vary in location according to whether the superior vena cava is obstructed above, below, or at the entrance of the azygos vein. Usually, the collaterals take one or more of 4 available routes: the internal mammary group of veins; the vertebral group of veins; the azygos vein; and the lateral thoracic group of veins.

Contrast material vena cavography is at present the principal method of demonstrating vena caval obstruction and the formation of collateral venous pathways.[2,8] This method has proven value as a diagnostic procedure and would be difficult to supplant. However, continued re-evaluation of older techniques in the light of newer and perhaps less hazardous diagnostic procedures is always desirable. In contrast material vena cavography, for example, 30 to 50 cc. of contrast material is injected. If a bilateral study is performed, as much as 60 to 100 cc. of material may be used. If such a large volume of material is injected under conditions of complete obstruction, the veins could rupture. Serial roentgenography is itself not without radiation hazard to the patient. Patient allergy to iodine is another possible disqualifying factor for contrast material vena cavography. These potential hazards, coupled with patient discomfort from the technique, seriously limit the use of vena cavography for repeated studies.

Recently, the scintillation camera has been used for visualizing vena cava obstruction.[5,7,9] Some advantages of the camera method are: (1) that the patient is exposed to a very low dose of radiation; (2) that only a small volume (1 to 2 cc.) of material is injected, if an isotope of high specific activity is used; and (3) that the patient experiences very little discomfort.

The object of the present study is to evaluate the scintillation camera as a noninvasive procedure for use with patients with superior vena caval syndrome due to intrathoracic neoplasm who are undergoing radiation treatment. Scintiphotographic evaluation was conducted (variously) before, during, and after the completion of radiation therapy.

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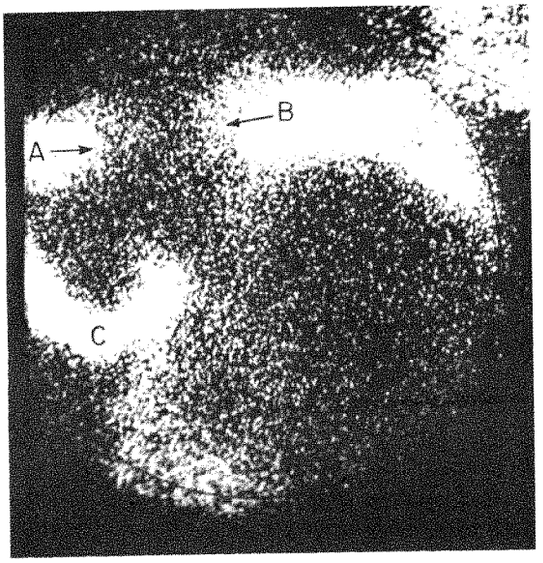


FIG. 1. Patient S.H. Squamous cell carcinoma of the esophagus with metastasis to the mediastinum manifesting superior vena caval syndrome. Scintillation camera vena cavogram demonstrates complete obstruction of the right (A) and left (B) innominate veins. A superficial cutaneous vein is seen (C) anteriorly on the right side.

MATERIAL AND METHOD

All 21 of the patients studied had known primary malignancies that caused superior vena caval syndrome. Most of the neoplasms were primary, nonresectable, intrathoracic malignancies requiring radiation treatment. Scintillation camera procedures were selectively used prior to, during, or after radiation treatment. In a few initial studies, confirmation was obtained by contrast material vena cavography.

The instrument used was the Anger scintillation camera (Phogamma/III, Nuclear Chicago); the isotope was Tc^{99m} pertechnetate. High specific activity Tc^{99m} (10 mc in 1 to 2 ml. volume) was drawn into 2 syringes. The patient was positioned sitting, facing the camera. The syringes containing 10 mc Tc^{99m} were each placed over the supraclavicular fossae, one on each side. The scintillation camera detector was positioned so that the syringes were just inside the periphery when viewed through the camera scope and the persistence scope. (The Polaroid shutter was closed so that the film was not exposed at the time of viewing through the camera scope.) When adjusted in this way, the passage of isotope through both subclavian veins, through the innominate veins, and finally in the superior vena cava could be visualized. Three second exposure scintiphotos were taken for 24 seconds. (The intensity for Tc^{99m} was set at 700. The pulse height analyzer was set to record Tc^{99m} with an energy range of 140 and a peak of 500.)

At the time of injecting the isotope, the patient's arms were held at, or raised above, the level of the shoulders to facilitate venous drainage. Two physicians, one on each side, injected the isotope simultaneously into the antecubital veins. Scintiphotos were taken immediately after isotope injection.

RESULTS

The passage of Tc^{99m} into the superior vena cava from both sides can be visualized simultaneously (Fig. 1; and 3–6). Figure 1 shows complete obstruction of the innominate veins on both sides (A, B). A superficial cutaneous vein is seen over the anterior part of the chest on the right side (C). These findings are confirmed by contrast material vena cavography (Fig. 2, *A* and *B*); tributaries of the innominate vein are visualized on both sides. In patient S.R., the studies were made before the initiation of irradiation. A partial obstruction of the left innominate vein and the subclavian vein was noted (Fig. 3). After cobalt 60 teletherapy over a 20 day period, there was complete relief of the left subclavian vein obstruction, but the obstruction of the left innominate vein persisted (Fig. 4). Patient J.H. had bronchogenic carcinoma and was being treated with irradiation. Partial obstruction of the right and left innominate veins was clearly demonstrated (Fig. 5). After cobalt 60 teletherapy the same patient showed complete relief of the right innominate vein obstruction, but the partial obstruction of the left innominate vein

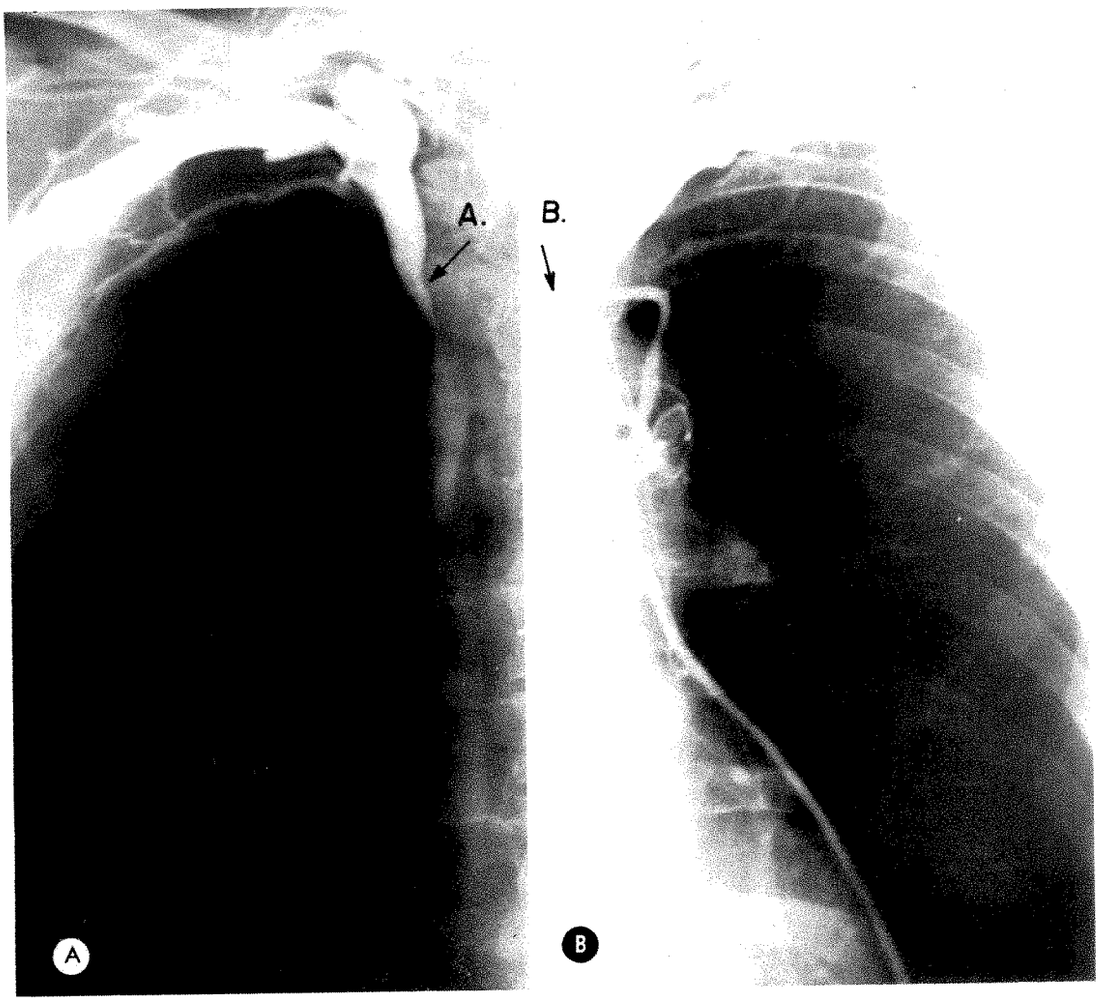


Fig. 2. (*A* and *B*) Contrast material vena cavograms of patient S.H. (Fig. 1), showing complete obstruction of the right (A) and left (B) innominate veins. The superficial cutaneous vein seen in Figure 1 is not seen in this study. Note that the level of obstruction of the 2 innominate veins is the same in both studies (A, B).

persisted (Fig. 6). Most of the patients had initial scintillation camera vena cavogram before irradiation. Partial or complete relief of obstruction duringor after irradiation was associated with clinical improvement in the form of relief of facial and upper limb edema. None of the patients studied complained of discomfort. The findings of a scintillation camera study of 1 patient made 10 days before death were confirmed at autopsy.[4] In this patient, the formation of collateral pathways between the internal mammary veins and the corresponding inferior epigastric veins was clearly demonstrated in the camera study.[4]

DISCUSSION

Superior vena cavography performed with the scintillation camera is a nonstressful, safe procedure that provides abundant useful information regarding the patency of venous pathways. It has been suggested that the scintillation camera study be considered a screening procedure on the claim that it can discriminate only major venous obstruction. By the technique described

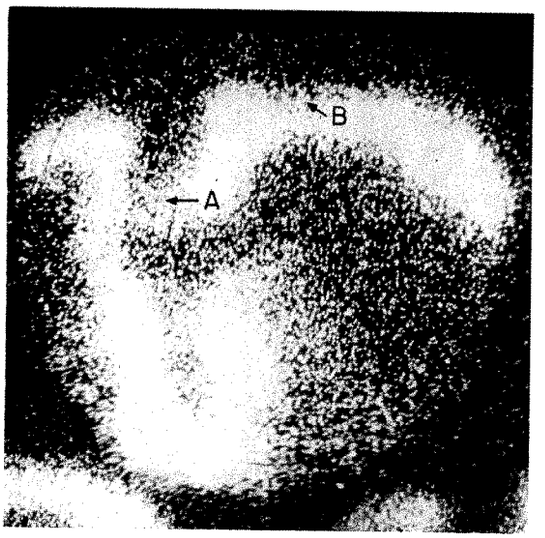


FIG. 3. Patient S.R. Oat cell carcinoma of the right bronchus with mediastinal metastasis. Scintillation camera vena cavogram demonstrates displacement of the course of the left innominate vein. There is partial obstruction of the left subclavian (B) and the left innominate vein near its junction with the superior vena cava (A).

above, however, it is possible to observe smaller tributaries and collateral venous pathways after superior vena caval obstruction.[4] In most cases, minute details of smaller veins are not necessary; the information obtained by scintillation camera is more than adequate. In those few cases where further details are needed, contrast material vena cavography can be used as a second procedure.

The cases illustrated in this paper clearly show that sufficient information is obtained by superior vena cavography with the scintillation camera to make it a valuable diagnostic procedure. Other attractive attributes of the technique include its safety and patient comfort. Total study time in each case is 2 to 5 minutes. The superior vena cava, innominate, and subclavicular veins on both sides are included in the same scintiphoto, thus saving both study time and Polaroid film. The small quantity of high specific activity Tc^{99m} pertechnetate used enables the study to be made without danger of venous rupture, even where there is complete venous obstruction.

Many patients with superior vena caval obstruction need radiation treatment. Knowledge of the actual status of venous patency is helpful in planning a course of

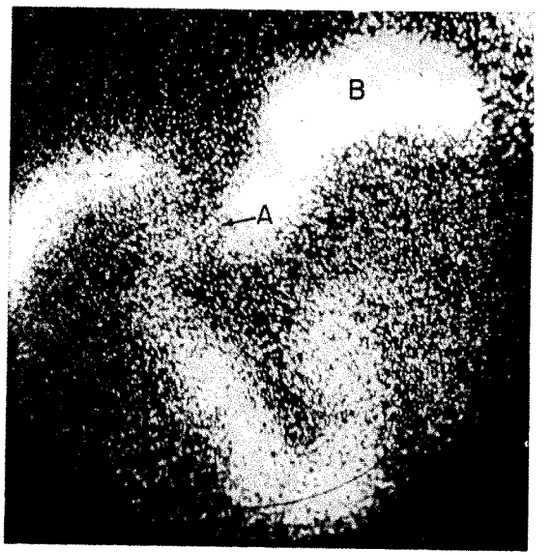


FIG. 4. Patient S.R. receiving cobalt 60 teletherapy. This study, made 20 days after that in Figure 3, shows complete obstruction of the left innominate vein near its junction with the superior vena cava (A). Note relief of the previous obstruction of the left subclavian vein (B) seen in Figure 3.

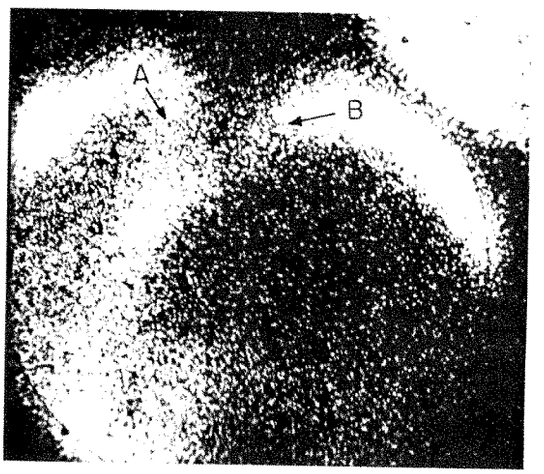


FIG. 5. Patient J.H. with bronchogenic carcinoma receiving cobalt 60 teletherapy. Scintillation camera vena cavogram shows partial obstruction of the right (A) and left (B) innominate veins.

treatment which avoids radiation injury to the patient's venous collateral channels. Once the treatment is started, a simple and safe procedure is needed for the repeated studies required to follow the course in each patient. Contrast material vena cavography is not an ideal procedure for repeated studies, owing to the inherent hazards and disadvantages mentioned earlier. On the other hand, scintillation camera Tc^{99m} vena cavography is simple, safe, and informative. It is the authors' opinion that the scintillation camera technique described should be considered as the procedure of choice for superior vena caval study, and that contrast material vena cavography should be reserved for special cases where more minute details are needed in the management of the patient.

SUMMARY

Obstruction of the superior vena cava and its tributaries and the response to radiation therapy were studied in 21 patients using the Anger scintillation camera after injecting 10 mc Tc^{99m} pertechnetate bilaterally and simultaneously in both arms. Partial and complete venous obstructions were demonstrated, and in a few cases a correlation was obtained with contrast material vena cavography.

The scintillation camera technique is simple, safe, and nontraumatic, and can be repeated frequently. The study can be performed even in cases where there is complete venous obstruction. Bilateral, simultaneous injection of Tc^{99m} saves study time and Polaroid film. Bilateral information is obtained in 1 scintiphoto.

It is suggested that the scintillation camera technique be used as the procedure of choice in cases of superior vena caval syndrome due to suspected partial or complete obstruction of the superior vena cava and its tributaries. This technique is useful in pre- and postirradiation evaluation of the superior vena caval syndrome.



FIG. 6. Patient J.H. This study was made 12 days after that in Figure 5, after completion of cobalt 60 teletherapy. Scintillation camera study shows complete relief of obstruction of the right innominate vein (A). Partial obstruction of the left innominate vein (B) still persists. Chest roentgenogram at this time showed partial regression of the tumor mass.

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INFERIOR PHRENIC ARTERY COLLATERALIZATION IN HEPATIC ARTERY OCCLUSION*

By GEORGE W. WIRTANEN, M.D.,† *and* JÜRI V. KAUDE, M.D.‡

THE inferior phrenic arteries usually originate from the aorta or celiac artery, and less frequently from the renal, hepatic or left gastric arteries. The roentgenographic anatomy of the phrenic arteries has been described in detail by Kahn.[8] They contribute to the arterial supply of the adrenal glands and are thus important in angiographic examinations for adrenal lesions.[8,9]

The purpose of the present paper is to discuss the role of the inferior phrenic arteries in arterial blood supply to the liver following occlusion of the hepatic artery, whether accidental or therapeutic.

MATERIAL AND METHOD

A total of 7 patients are included. Four patients had thrombosis of the celiac axis distal to the origin of the inferior phrenic arteries. The occlusion was secondary to catheterization for continuous chemotherapeutic infusion for metastatic tumors in the liver. One patient had hepatic artery ligation at resection of the left and caudate liver lobes for primary cholangiocarcinoma. One patient had undergone dearterialization of the liver[2] for hepatic metastases of a small bowel carcinoid, and one patient had therapeutic hepatic artery ligation for traumatic arterioportal aneurysm.[11] All patients were examined with selective angiography of the inferior phrenic arteries and serial filming 3 weeks to 4 months following celiac or hepatic artery occlusion.

RESULTS

The inferior phrenic arteries originated from the celiac artery in 4 patients and had a common trunk in 2. In 2 patients the origin of the common inferior phrenic artery trunk was in the aorta, and in 1 patient the right inferior phrenic artery examined originated from the left gastric artery.

In all patients, rearterialization of the liver, or parts of the liver, via the inferior phrenic arteries was demonstrated. The arteries were hypertrophic and tortuous with a maximal width of 5 mm. They appeared to supply the liver either directly via anterior or posterior branches, or had anastomosed with hepatic arteries distal to occlusion (Fig. 1–4). In incomplete hepatic artery occlusion there was still hypertrophy of the inferior phrenic artery with segmental hepatic artery opacification (Fig. 3). In 1 patient resupply of a metastatic tumor nodule by the inferior phrenic artery was demonstrated (Fig. 1*B*).

In 3 patients it was shown that collateral arterial flow to the liver was also developed from the dorsal pancreatic artery (Fig. 1*C*), from arteries of a jejunal loop (Fig. 2*B*), or superior mesenteric and left gastric arteries.

There was no mortality attributable to hepatic necrosis following hepatic artery occlusion in the present series of patients, 6 of whom had hepatic tumor. In 1 patient, as reported previously,[11] ligation of the hepatic artery resulted in healing of an arterioportal fistula.

DISCUSSION

Hepatic artery occlusion secondary to surgical trauma has been reported to produce moderate or serious morbidity but it is not necessarily fatal.[5,10]

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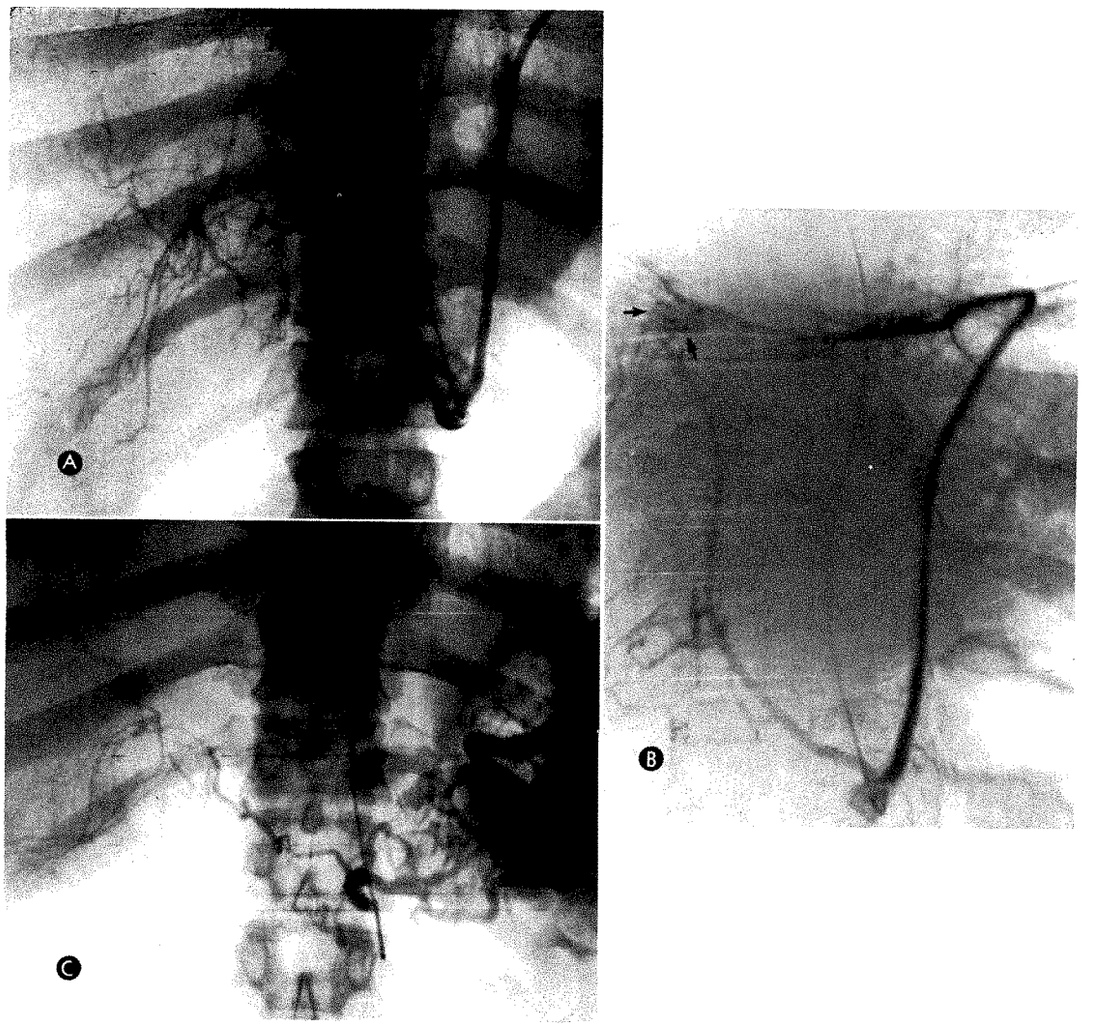


FIG. 1. This 39 year old patient with metastatic adenocarcinoma of the colon had thrombosis of the celiac axis distal to the inferior phrenic artery trunk. Both inferior phrenic arteries are dilated and measure 5 mm. in diameter. (*A*) In the early arterial phase, extensive collateralization to the liver is present. (*B*) The left inferior phrenic artery collaterals supply a hypervascular tumor nodule lying to the right of the spine. This vessel was infused with cytotoxic agents for 3 weeks. (*C*) Additional arterial supply is provided by the dorsal pancreatic artery arising from the superior mesenteric artery. The splenic artery fills through pancreatic collaterals.

Arterial flow to the liver is re-established as early as 4 days after hepatic artery ligation.[2] One of the collateral pathways for an adequate arterial blood supply to the liver allowing survival of the animal in experimental hepatic artery occlusion in dogs is the inferior phrenic artery.[7] In man this collateralization of the inferior phrenic artery following hepatic artery occlusion has been reported by Graham and Cannell,[5] Düx *et al.*,[4] Kaude *et al.*,[11] and Bengmark and Rosengren.[2] Although by no means the only collateral pathway[13,14] (Fig. 1*C*; and 2*B*), the marked increase of its caliber shows the importance of the inferior phrenic artery for arterial blood supply to the liver. This arterial blood supply is sufficient for the normal liver parenchyma, as it suffers minor damage after hepatic artery ligation with only transitory alteration of

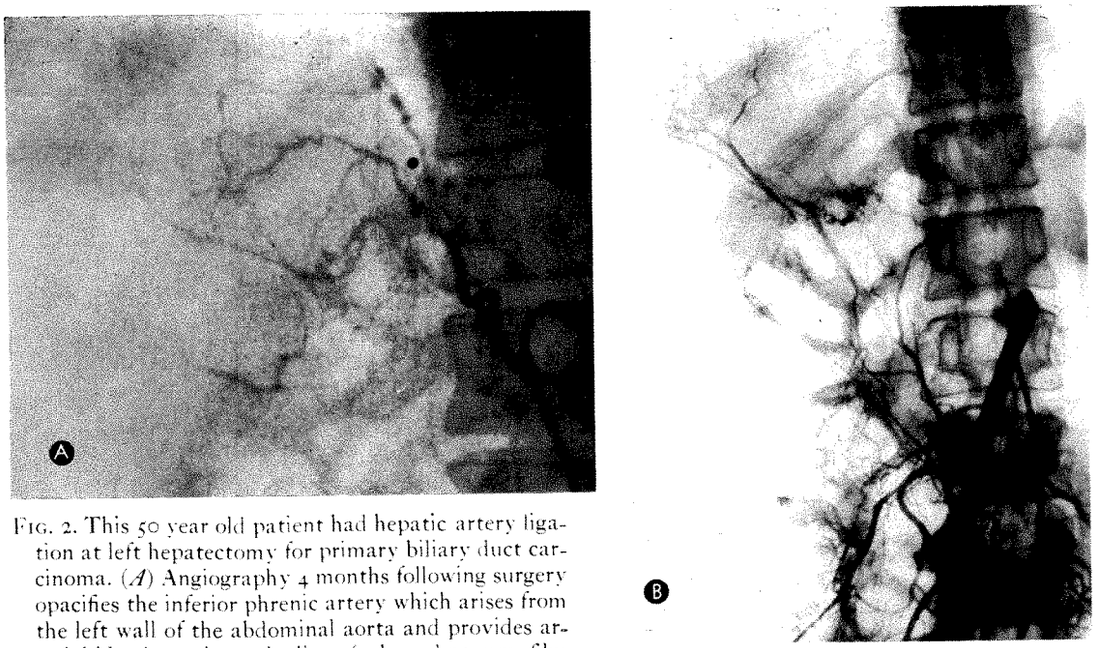


FIG. 2. This 50 year old patient had hepatic artery ligation at left hepatectomy for primary biliary duct carcinoma. (*A*) Angiography 4 months following surgery opacifies the inferior phrenic artery which arises from the left wall of the abdominal aorta and provides arterial blood supply to the liver (enlarged 70 mm. film exposed from output screen of image intensifier). (*B*) There is also segmental hepatic artery opacification with contrast medium injected into the superior mesenteric artery. These collaterals are developed from arteries of the jejunal loop which was used for choledochojejunostomy.

liver functions.[4,12,15] The diminished arterial blood supply probably also results in greater portal vein dependence for liver parenchymal metabolism, which further reduces the effects of arterial ischemia to the normal liver. Thus, it may well be that the hepatic artery occlusion in itself is not responsible for an eventual fatal outcome, but infection, underlying disease and surgical procedures are contributing factors to the death of the patient.[5,10]

In the presence of hepatic tumor, occlusion of the hepatic artery and even dearterialization of the liver with ligation of hepatic arteries, and arteries presenting potential collateral pathways to the liver do not result in patient death, and the method has been used for palliation in patients with metastatic lesions in the liver, or as pretreatment for liver resection of metastatic cancer.[1,2,12,15] Metastatic tumors in the liver are probably more sensitive to arterial ischemia than the normal liver parenchyma because they depend entirely on the arterial blood supply[3,6] and cannot compensate their metabolic needs by increased portal vein flow. Dearterialization does result in tumor ischemia and also in necrosis to a variable extent, but the surviving cells of a malignant tumor still require arterially supplied metabolites for their physiologic demands, and collateral vessels necessary for growth of residual tumor will develop. Indeed, the tumor blood supply by the inferior phrenic artery following hepatic artery occlusion was demonstrated in 1 patient (Fig. 1*B*), indicating that tumor ischemia produced by hepatic artery occlusion was only transitory.

Palliation in malignant liver tumors can also be achieved by hepatic artery infusion with cytotoxic agents.[16] During such continuous infusion over several weeks, thrombosis of the hepatic artery may occur. This results in loss of the artery used for therapy. Occasionally, the collateral vessels which develop following arterial occlusion have sufficient caliber to accommodate a reinfusion catheter (Fig. 1, *A* and *B*), but more generally multiple small collaterals develop

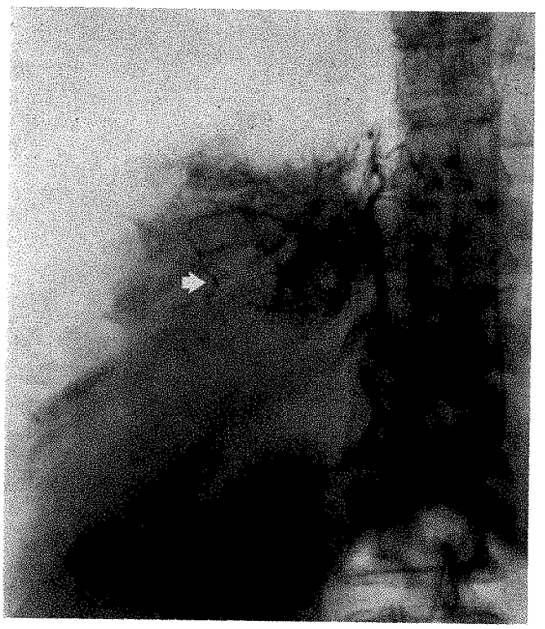


FIG. 3. A 59 year old patient with metastatic breast carcinoma had partial (approximately 90 per cent) occlusion of the hepatic artery following a 3 week course of intra-arterial chemotherapeutic infusion. Selective angiography of the right inferior phrenic artery originating from the aorta demonstrates well developed collateral vessels to the liver. (Arrow points to a collateral branch of the hepatic artery.)

(Fig. 1*C*; and 2*B*), which, even if they can be catheterized selectively, are not suitable for prolonged infusion therapy. However, if the hepatic artery has been occluded, catheterization of the inferior phrenic artery should be attempted for continued infusion.

It is important to know that hypertrophy of the inferior phrenic artery does not occur only following hepatic artery occlusion. It may also develop secondary to inflammatory conditions of the pleura, as we have seen dilated tortuous vessels from the posterior branch of the inferior phrenic artery supply pleural adhesions following pleurisy or hemothorax. The right inferior phrenic artery originating from the renal artery or aorta may also participate in collateral arterial flow to the liver in the presence of celiac artery stenosis.

The inferior phrenic artery was recognized in 1933 as a significant hepatic collateral pathway.[5] As such, it has gained importance in therapeutic hepatic artery ligation for palliation in malignant hepatic tumors, and it is a possible pathway for intra-arterial infusion therapy following hepatic artery occlusion. However, occlusion or ligation of the hepatic artery may

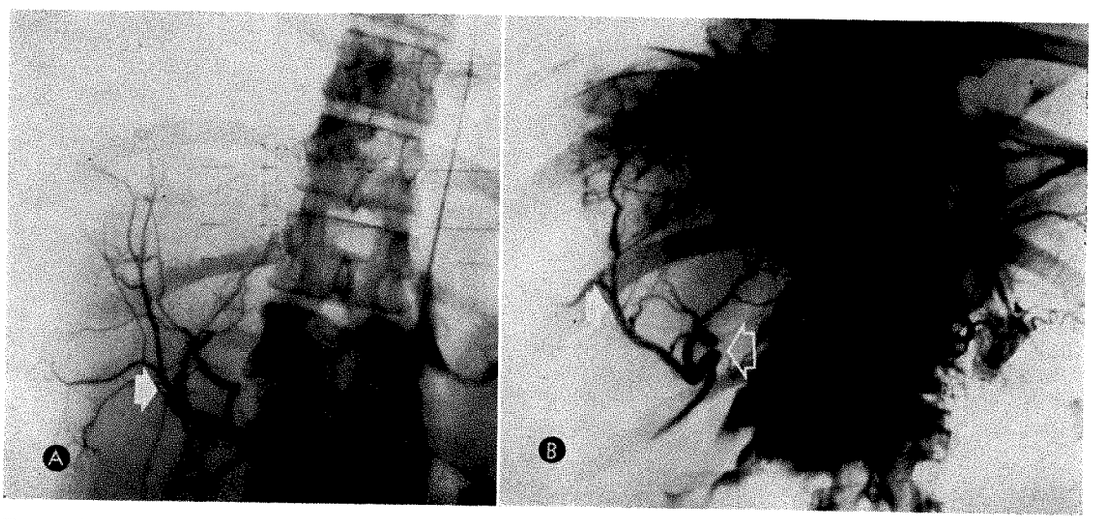


FIG. 4. A 45 year old patient with metastatic breast cancer. (*A*) There are several stenotic areas in the hepatic artery. The artery was occluded by prolonged chemotherapeutic infusion. The arrow demonstrates an artery in the right lobe which is also filled at (*B*) selective inferior phrenic angiography following occlusion of the hepatic artery. Open arrow indicates the loop of hepatic artery which fills via collaterals developed from the right inferior phrenic artery.

reduce the effectiveness of the intra-arterial infusion therapy, or may make it impossible, because collateral pathways which develop and contribute to the arterial supply of the tumors may be too small for prolonged infusion therapy.

SUMMARY

Seven patients who had thrombosis of the hepatic artery secondary to prolonged intra-arterial infusion of cytotoxic drugs, or had hepatic artery ligation, demonstrated significant inferior phrenic artery collateralization to resupply the liver and eventually the metastatic tumor nodules.

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CARCINOMA OF PANCREAS—PALLIATIVE RADIOTHERAPY*

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THERE are few cases of potentially curable carcinoma of the pancreas. Most cases are considered only for palliative therapy.[1,4] The therapeutic goals for palliation have included increased longevity, decreased abdominal mass, decreased jaundice and relief of pain. Radiotherapy has been employed for palliation. The efficacy of radiotherapy has been questioned.[3,5,6,8]

We analyzed our experience with palliative radiotherapy for carcinoma of the pancreas, adhering to the definition of palliation as "soothing without really curing."[9] The experience suggested that a high incidence of therapeutic benefit could be achieved with modest dosages of irradiation.

MATERIAL AND METHOD

Between 1964–1971, 20 cases of pancreatic carcinoma were treated with radiotherapy for the chief complaint of pain at the Hospital of the Good Samaritan Medical Center. Between 1947–1971, 2 cases were treated at LAC/USC Medical Center. The records were reviewed and the key information extracted.

The diagnosis of pancreatic carcinoma was made by the surgical findings of a mass in the pancreas in all cases. Eleven cases had proven liver metastases. A biopsy of the mass was done in 8 cases and a biopsy of the adjacent lymph nodes or liver nodules was done in 14 cases. Eight cases had a concomitant biliary diversion procedure. Twelve cases were poorly differentiated carcinoma; 4 cases were well differentiated; and 6 cases were not classified. Seven cases came to autopsy. The autopsy findings confirmed the diagnosis of pancreatic carcinoma in the 7 cases.

Twenty cases were treated with cobalt 60 teletherapy and 2 cases were treated with 240 kv. roentgen therapy. Twelve cases received concomitant 5-fluorouracil. Nine cases were treated with an initial loading dose of 5-fluorouracil; 3 of the cases without the initial loading dose.[2,7]

The case material was divided into 2 groups according to response to therapy. Group one had significant alleviation of pain and a documented reduction in the potency and frequency of analgesic requirements. Group two had neither improvement of pain nor reduction of analgesic requirements. Parameters studied were the total irradiation dosage given, the dosage at which a favorable response was observed, the effect of concomitant 5-fluorouracil and the relation of liver metastasis and histopathology to response.

RESULTS

Seventeen of the 22 patients had significant alleviation of pain with radiotherapy; 6 of these patients had an antecedent biliary drainage procedure. The tumor dose administered in this group varied from 600 rads/4 days to 5,000 rads/48 days. The average tumor dose for a favorable response was 1,440 rads/14 days (Table 1). The mean survival time from date of initial radiotherapy was 67 days.

Five of the 22 patients did not have significant alleviation of pain with radiotherapy; 2 of these patients had an antecedent biliary drainage procedure. The

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TABLE I

TUMOR DOSE TO ALLEVIATE PAIN

Less Than 800 Rads	800–1,600 Rads	1,600–2,400 Rads	More Than 2,400 Rads
500 rads/ 7 days	1,053 rads/10 days	1,840 rads/ 12 days	2,590 rads/29 days
600 rads/ 5 days	1,071 rads/ 8 days	1,925 rads/ 15 days	3,159 rads/26 days
675 rads/ 8 days	1,305 rads/14 days	2,100 rads/ 9 days	
675 rads/12 days		2,400 rads/ 15 days	
700 rads/ 9 days		2,400 rads/136 days	
720 rads/ 9 days			
750 rads/10 days			

total tumor dose varied from 650 rads/6 days to 5,000 rads/57 days. The mean survival time from date of initial treatment was 39 days.

Nausea was observed by 9 patients prior to radiotherapy. With radiotherapy 3 additional patients developed nausea; however, 2 patients had less nausea.

Twelve cases received 5-fluorouracil; 8 had significant palliation. Ten cases did not receive 5-fluorouracil; 9 had significant palliation (Table II).

Eleven cases had liver metastasis; 8 of the 11 cases had significant palliation (Table III). Five of these 8 cases also had received 5-fluorouracil.

Cases with either poorly differentiated carcinoma or nonclassified carcinoma had a high incidence of favorable response. Cases with well differentiated carcinoma had a low incidence of response (Table IV).

DISCUSSION

Patients with carcinoma of the pancreas commonly have distressing pain.[1,4] The management of pancreatic carcinoma pain can be difficult. Surgical management has been reported to be worthwhile. Biliary drainage procedures have alleviated pain in patients with or without jaundice.[6]

The radiotherapeutic management of pancreatic carcinoma pain has not been well accepted. Falkson and Falson[5] have suggested that it may be worthwhile, but only with concomitant 5-fluorouracil. Miller and Fuller[8] believe that radiotherapeutic doses of 5,000 rads or more should be considered, especially if an improvement in the duration of survival is to be sought.[2] However, radiotherapeutic doses of this magnitude, administered to the upper abdomen, can cause adverse reactions that are difficult to accept in patients with almost no expectancy of cure and a predictably short life expectancy. In our series, significant alleviation of pain was usually achieved with a tumor dose of less than 1,600 rads. Most cases had poorly differentiated carcinoma. The presence of liver metastasis did not interdict a favorable response. We were unable to

TABLE II

EFFECT OF CONCOMITANT 5-FLUOROURACIL ON THE RESPONSE TO RADIOTHERAPY

	Pain Palliation	No Pain Palliation
5 Fu 12/22	8/12	4/12
No 5 Fu 10/22	9/10	1/10

TABLE III

EFFECT OF LIVER METASTASIS ON THE RESPONSE TO RADIOTHERAPY

	Pain Palliation	No Pain Palliation
Liver Metastasis 11/22	8/11	3/11
No Liver Metastasis 11/22	9/11	2/11

TABLE IV

INFLUENCE OF HISTOPATHOLOGY ON THE RESPONSE TO PALLIATIVE RADIOTHERAPY

Histopathology	Pain Palliation	No Pain Palliation
Well differentiated carcinoma	1/4	3/4
Poorly differentiated carcinoma	11/12	1/12
Not classified carcinoma	5/6	1/6

substantiate the efficacy of concomitant 5-fluorouracil.

Nausea was a frequently observed symptom prior to radiotherapy. At radiotherapeutic dose levels that induced pain relief, nausea was infrequently made worse and occasionally improved.

Radiotherapy has not been shown to prolong life. Therefore, for purpose of palliation, the administration of low tumor dosage, if efficacious, is proper. The total number of cases in the study precludes unequivocable conclusions. However, the results do suggest that a trial of palliative radiotherapy, with tumor dosages that are modest, given over a relatively short period of time can significantly improve the quality of life in cases with painful, poorly differentiated pancreatic carcinoma.

SUMMARY

The efficacy of radiotherapy in the management of pain caused by pancreatic carcinoma was assessed.

Radiotherapy was infrequently employed to alleviate pain. However, when employed, radiotherapy almost uniformly alleviated pain at low dose levels that were well tolerated.

The presence of liver metastasis did not interdict a favorable response.

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CLINICAL DECISIONS IN THE MANAGEMENT OF STAGE I ENDOMETRIAL CARCINOMA*

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CARCINOMA of the endometrium, Stage I, is defined by the International Federation of Gynecology and Obstetrics, as carcinoma confined to the body of the uterus. The value of irradiation as an adjuvant to surgery in the management of this cancer has been under controversy for many years. As was pointed out by Gusberg and Yannopoulos[5] and others, this Stage I contains such a heterogeneous collection of patients that comparison of treatment protocols and survival rates among the various investigators is difficult. Patients with more favorable prognostic characteristics have tended to be treated by surgery alone. Certain authors have used this to imply that adjuvant irradiation is of little use in Stage I carcinoma since their results with surgery alone have been so favorable.

It is attempted in this study to describe a series of prognostically distinct groups which are homogeneous in most features. Thus, the most important variable, it is hoped, is therapy and the success of the various treatment regimens will be more easily comparable.

MATERIAL AND METHOD

Between 1940 and 1963, 837 primary cases of endometrial carcinoma confined to corpus (clinical Stage I) were treated at the Roswell Park Memorial Institute. However, in only 790 of these were histologic slides available for grading purposes and complete clinical data necessary for the undertaking of this study. Irradiation was the primary treatment in 265 cases and surgery in 525 cases (of which 510 cases had total hysterectomy and 15 cases subtotal hysterectomy). None of these patients were lost to follow-up for at least 5 years post diagnosis.

Grading of tissue preparation was carried out as follows: Grade 0, adenoacanthoma; Grade 1, well-differentiated adenocarcinoma; Grade 2, intermediately differentiated adenocarcinoma; and Grade 3 poorly differentiated adenocarcinoma. The 5 year crude survival rates were 74, 65, 51 and 44 per cent, respectively.

The age was divided into 4 ranges: less than 50, 50–59, 60–69 and 70 years and older; and these were associated with significantly varying 5 year survival rates of 81, 68, 59 and 42 per cent, respectively.

Uterine cavity depth and uterine size were both weakly discriminant with respect to prognosis and were well correlated with each other. Therefore, only the former measurement was employed. Uterine cavity depths of 9 cm. and 10 cm. were associated with 5 year survival rates of 56 and 50 per cent, respectively.

Histologic grade, age and uterine cavity depth then were selected to subclassify the Stage I corpus carcinoma patients into 7 prognostic classes. The procedure of subclassification has been published elsewhere.[7]

The Wilcoxon rank-sum, student t, Fisher exact, and chi-square tests were employed on the appropriate occasions. The Berkson-Gage actuarial method was used for estimations of survival, cancer mortality and persistence-recurrence rates.

RESULTS

Table 1 shows that patients with Stage I

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TABLE I

PROGNOSTIC CLASSES IN STAGE I CARCINOMA OF CORPUS UTERI

Prognostic Class	No. of Cases	Per Cent of Cases		
		Five Year Survival* (per cent)	Cancer Mortality* (per cent)	Persistence Recurrence* (per cent)
A 50 years Grade 0 or 1	84	86	8	17
B 50–69 years Grade 0	44	77	11	11
C 50–69 years Grade 1	348	66	12	16
D 70 years Grade 2 or 3 9 cm. cavity	99	61	23	23
E 70 years Grade 0 or 1	117	49	14	20
F 70 years Grade 2 or 3 10 cm. cavity	35	34	31	31
G 70 years Grade 2 or 3	62	33	42	48
All Cases	790	61	17	20

* Crude 5 year survival rates decrease, and relative cancer mortality and persistence-recurrence incidence, 0 to 5 years post-diagnosis, increase with class A through G (p .02 to .001).

endometrial carcinoma consist of a broad spectrum of groups of patients with significantly different degrees of prognoses. It is seen that classes A through C groups of patients are arranged in decreasing order of survival. The discrepancy occurring in the order of cancer mortality and recrudescence rates for classes D and E is slight. This is explained presumably by the higher incidence of concurrent disease deaths in Class E because of the advanced age of patients, and the lower incidence of cancer deaths or of recurrence because of their lower grade of malignancy.

Class A consists of young patients (less than 50 years of age) with low grade cancer (0 or 1). The crude 5 year survival rate is 86 per cent with only 8 per cent of deaths due to corpus cancer, and with 17 per cent of cases having had persistent or recurrent cancer. This means that survival corrected for noncancer deaths is 92 per cent and that 9 per cent (or half of the cases that had persistence or recurrence) was salvaged within 5 years post treatment. The procedures of retreatment and results for recurrent corpus cancer have been published previously.[7]

Class B consists of middle-aged patients (50–69 years) with adenoacanthoma and has the next best survival rate of 77 per cent. Eleven per cent had recrudescence of disease. None of these were salvaged. The corrected survival rate is 89 per cent.

Class C makes up nearly half (44 per cent) of the cases with localized cancer, consisting of middle-aged patients with Grade 1 lesions. The survival rate is 66 per

TABLE II

CLINICAL FINDINGS AND PROGNOSIS ACCORDING TO TREATMENT IN STAGE I CARCINOMA OF CORPUS UTERI

Clinical Findings	Treatment Groups		
	Irradiation Only	Surgery	Preoperative Irradiation
No. of cases	265	130	395
Mean age (yr.)	65+	60−	60−
Mean weight (lb.)	180+	168−	177+
Hypertension (%)	54	55	53
Diabetes (%)	19	16	16
A.S.H.D. (%)	51+	25−	17−
Medically inoperable (%)	93+	4−	8−
Persistent or recurrent disease (%)*	27+	26+	14−
Local disease (%)*	25+	25+	8−
Crude 5 year survival (%)	47−	59+	73++
Cancer deaths (%)	22+	17	12−

+ Indicates values significantly higher than those indicated by −, ++ indicates values higher than those indicated by + and those indicated by − for each of the findings (p .02).

* Disease persistent or recurrent 0 to 5 years post treatment. Local disease includes cases with persistent or recurrent lesions in corpus or vagina with or without pelvic or distant spread.

A.S.H.D. = arteriosclerotic heart disease.

cent with 12 per cent dying of cancer. Sixteen per cent of cases had recrudescence of disease of which one-fourth (or 4 per cent of the total) were controlled by subsequent treatment. The corrected survival rate is 89 per cent.

Class D consists of non-elderly patients (less than 70 years of age) with high grade lesions (2 or 3) and with normal or small uteri (cavity depth less than 10 cm.). Survival is 61 per cent with 23 per cent dying of uncontrolled or recurrent cancer. The corrected rate is 77 per cent.

Class E consists of elderly patients (more than 69 years) with low grade cancers. Because of advanced age, the crude survival rate is only 49 per cent; however, when corrected for noncancer deaths the rate is 86 per cent, nearly as good as that of Class C. Twenty per cent of cases had recrudescence of which one-third (or 6 per cent of the total) were salvaged.

Class F consists of non-elderly patients with high grade lesions and with large uteri (cavity depth greater than 9 cm.). Survival rate is low (34 per cent) with 31 per cent of cases dying of cancer. None of these that persisted or recurred were saved. The corrected rate is 69 per cent.

Class G with the lowest survival rate of only 33 per cent consists of elderly patients with high grade lesions. The death rate due to cancer is 42 per cent with a corrected rate of 58 per cent. Nearly half of the cases had recrudescent disease and only one-eighth of these were salvaged.

Table II shows the differential clinical features and course of patients subjected to 3 different regimens: primary irradiation; hysterectomy; and irradiation followed by hysterectomy (except for less than 3 per cent who had a subtotal hysterectomy procedure).

Patients treated with irradiation only are elderly and poor operative risks, primarily due to cardiovascular disease; survival is the lowest of the 3 treatment groups due to the high incidence of concurrent disease deaths (31 per cent).

Patients treated with total or subtotal hysterectomy initially had lower average weights. Their survival is intermediate in position, but its persistence or recurrence rate is similar to those treated with irradia-

TABLE III

METHODS OF MANAGEMENT OF STAGE I CARCINOMA OF CORPUS UTERI

Treatment Techniques	Irradiation Only	Surgery	Preoperative Irradiation
No. of cases	265	130	395
Surgery			
Total hysterectomy	—	96	98
Subtotal hysterectomy	—	4	2
Uterine radium			
Multiple tubes	56	—	36
Tandem	44	—	64
Mg.-hr. (1×10^2), mean	48	—	57
Vaginal radium	3	27	2*
Mg.-hr. (1×10^2), mean	29	30	16
X-ray therapy	56	28*	16*
Pelvic dose (1×10^2 r), mean	40	36	28
Point A dose (1×10^2 r), mean	64	34	59

* Postoperative irradiation.

tion. Cancer mortality is intermediate and is not different from those of the other 2 groups.

The group receiving preoperative irradiation has the best survival, and the lowest cancer morbidity and mortality rates. Except for the greater mean body weight the clinical characteristics of this group are similar to those of the surgical group.

Table III shows the radiation technique employed and doses administered. More than half of patients received intrauterine radium using the Heyman packing technique (56 per cent in the irradiation only group and 36 per cent in the preoperative irradiation group). Patients with small uterine cavities received radium *via* the radium applicator. Two applications of 2,000 to 3,000 mg.-hr. each, were made 2 to 4 weeks apart, lower doses being given with tandem applicators. On the average, most patients in the preoperative irradiation group received a total dose close to 6,000 mg.-hr. In the irradiation only group, patients who received external irradiation received lower radium doses. Thus, the mean dose was less than 6,000 mg.-hr.

Total hysterectomy was the definitive surgical procedure in the majority of cases (97 per cent). Subtotal hysterectomy was employed in 14 patients and they all received postoperative irradiation. In the surgical group 57 patients had hysterectomy alone, 30 had hysterectomy plus radium, 37 had hysterectomy plus roentgen therapy and 6 had subtotal hysterectomy plus radium. In the preoperative irradiation group 342 patients had radium applications before surgery. The 9 who had subtotal hysterectomy also received postoperative roentgen therapy in addition. Of the others, 40 patients received roentgen therapy plus radium and 13 only roentgen therapy before hysterectomy.

Vaginal radium sources in colpostats, plaques or ovoids were seldom used in the irradiation only and preoperative irradiation groups. Some 27 per cent of the surgical group received postoperative vaginal radium to a mean dose of 3,000 mg.-hr. Full pelvis roentgen therapy of approximately 4,000 r in 4 weeks, was administered in 56 per cent of the irradiation only group and postoperatively, in 28 per cent of the

surgical and in 16 per cent of the preoperative irradiation groups to approximately 3,000 r in 3 weeks. The major indications for postoperative roentgen therapy were invasive cancer deep in the myometrium or outside the corpus in the fallopian tubes, ovaries and/or pelvic lymph nodes.

The average doses to Point A were estimated as 6,400 r in the irradiation only, 3,400 r in the surgical, and 5,900 r in the preoperative irradiation groups. The low Point A dose in the surgical group is due to the fact that in about half of the cases receiving postoperative irradiation, vaginal radium was administered only for prophylaxis. The radium dose for such cases was usually 2,000 to 3,000 mg.-hr.

Figure 1 illustrates graphically the monotonic decrease in crude 5 year survival rates from Class A through G groups of patients, treated with irradiation only, surgery or preoperative irradiation.

Among the 3 treatment modalities the preoperative irradiation method is associated with the best survival for Classes C through F as illustrated in Figure 2. The observed variations are not significant for end classes A (patients less than 50 years with low grade lesions) and B (patients 50–69 years with adenoacanthoma) and for Class G (patients over 69 years with high grade lesions).

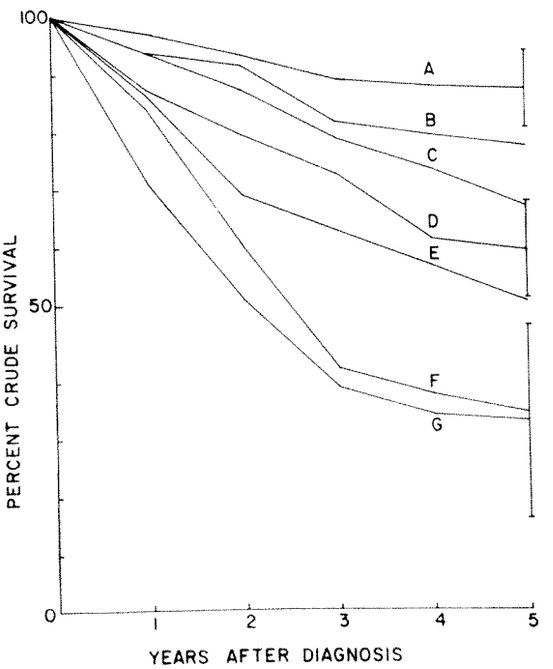


FIG. 1. Survivorship in prognostic classes of Stage I carcinoma of the corpus uteri. Vertical bars indicate ±2 standard errors.

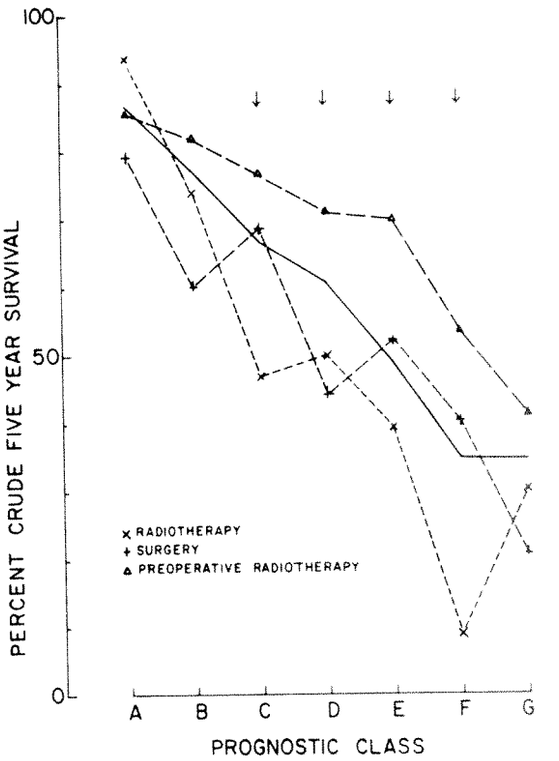


FIG. 2. Crude 5 year survival rates for prognostic classes according to treatment. The variations among treatment groups within prognostic classes indicated by arrows are significant ($p < 0.05$).

Figure 3 shows that persistence or recurrence of disease at all sites (local, distant or both) within 5 years post diagnosis differs among treatment groups within Classes C, D and G. It is highest for patients treated by irradiation in Class C (50–60 years, Grade 1) and for those treated surgically in Classes D (less than 70 years, less than 10 cm. cavity, high grade lesions) and G (over 69 years, high grade lesions). Local disease in corpus, cervix, and/or vagina with or without regional pelvic or distant spread at one time or another within the 5 year

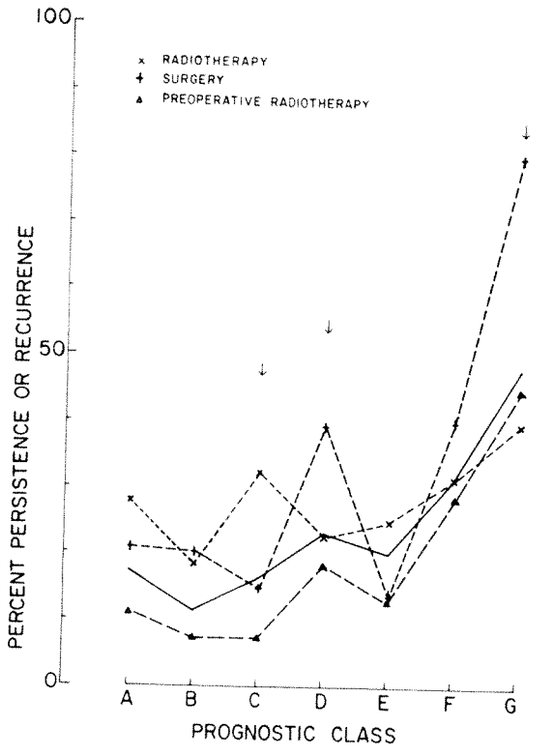


FIG. 3. Five year persistence or recurrence rates for prognostic classes according to treatment. The variations among treatment groups within prognostic classes indicated by arrows are significant ($p < 0.05$).

period, had a similar variation as for all sites above, except that in the high grade lesions the preoperative irradiation group had a lower incidence of recurrence of local disease.

Figure 4 indicates that deaths due to cancer differ among treatment groups within Classes C, D and G in a similar manner as in cancer persistence or recurrence rates.

The complication rate was low. There were only 2 cases of rectovaginal fistulas in the irradiation only group, and only 50 cases of postoperative wound complications without relationship to the type of adjuvant irradiation.

The results of this study can be summarized as follows: (1) endometrial carcinoma confined to corpus consists of groups of individuals with a wide range of prognoses; (2) common clinico-pathologic factors such as age, histologic grade and uterine cavity depth can be used to classify these patients into distinct prognostic groups; (3) in general, the results of preoperative irradiation in the management of these patients are superior to those of surgery with or without postoperative irradiation, survival and incidences of recurrent disease and of cancer deaths being less when irradiation is administered prior to surgery; (4) irradiation alone is employed in patients who are of poor surgical risk, survival being low because the majority of cases die of concurrent disease, and the recurrence persistence rate is similar to that of the surgical group, but the proportion of failures having been salvaged is less; (5) operable patients who are young (less than 50 years of age) with low grade lesions and patients with adenoacanthomas show only slight improvement,

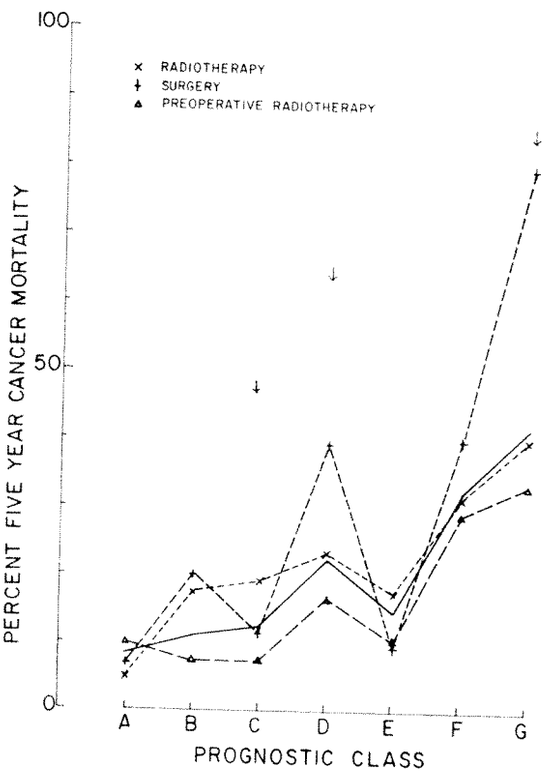


FIG. 4. Five year cancer mortality for prognostic classes according to treatment. The variations among treatment groups within prognostic classes indicated by arrows are significant ($p < 0.05$).

when preoperative irradiation is administered; and (6) operable patients who are middle-aged (50–69 years) with Grade 1 lesions and patients with high grade lesions fare significantly better, when preoperative irradiation is employed.

DISCUSSION

The survival and course of patients with carcinoma of the endometrium are affected by various factors. Thiede and Lund[16] found in their group of patients that age at diagnosis, uterine bulk and depth, degree of tumor anaplasia, depth of tumor invasion, and cardiac status were statistically significant in determining survival. Nolan *et al.*[12] showed that patients with smaller uteri had a better chance of survival than those with larger uteri. Morris *et al.*,[10] and Gusberg and Yannopoulos[5] had similar findings.

Many factors influence uterine size, including parity, presence of fibroids, menopausal status, and size of the tumor. It has been suggested that larger, more friable tumors, metastasize more easily; in addition, it is an indication that the tumor has been present a long time and therefore is more likely to have spread.

Lampe,[8] Nolan *et al.*,[12] Climie and Rachmaninoff[2] and others have correlated histologic grade and prognosis. The poorer prognosis for the more anaplastic lesions is probably related to their increased ability to invade the lymphatics and to their potential for myometrial penetration. Nolan *et al.*[12] illustrated that patients with large or small uteri with high or low histologic grade tumors had better survival rates following preoperative irradiation and surgery rather than surgery alone. Speed[15] tried to show with a relatively small number of cases that in histologic Grades 2 and 3, a greater survival rate occurred after surgery alone than after irradiation in combination with surgery.

Older patients with carcinoma of the corpus uteri have less chance of survival. This is related to the fact that the incidence of degenerative diseases such as arteriosclerotic cardiovascular disease, hypertension, diabetes and others, increases with age. In the series of Morris *et al.*[10] the median age was 59.2 years, in Speed's[15] series it was 55 years, and in the series of Marcial *et al.*[9] it was 58.7 years.

A staging system based on uterine size and depth, histology of the tumor, and cervical involvement was discussed by Gusberg and Yannopoulos.[5] The value of preoperative irradiation in Stage 1 carcinoma of the uterus is still subject to controversy. The objectives of irradiation include induction of uterine shrinkage, rendering hysterectomy easier, and devitalization of the tumor so that recurrence, as well as implantation, is less likely to occur. Graham[4] reviewed the literature on endometrial cancer and found an 8 per cent average recurrence rate reported in patients treated with surgery alone *versus* 3 per cent average recurrence rate in those given preoperative radiation therapy.

Table IV summarizes the representative 5 year survival rates in Stage 1 carcinoma of the endometrium reported by various authors. The summary shows a 77 per cent 5 year survival rate for preoperative irradiation followed by hysterectomy *versus* 73 per cent 5 year survival for surgery alone. It is assumed that the patients with small uteri and low-grade tumors were more likely to have undergone surgery—a tendency demonstrated by Nolan *et al.*[12] in their study. Thus the difference in treatment becomes more significant. The trend in the recent literature[5,9,12] is toward the use of preoperative radiation therapy and surgery in the treatment of Stage 1 carcinoma of the endometrium. Graham,[4] in a preliminary report of a randomized study, showed 76 per cent 5 year survival using preoperative irradiation and surgery *versus* 81 per cent 5 year survival using surgery followed by radiation therapy as compared to 64 per cent 5 year survival utilizing surgery alone. His data suggest that adjuvant radiotherapy is of some value whether given pre- or postoperatively. Since these factors seem to be the most important, we

TABLE IV

REPRESENTATIVE 5 YEAR SURVIVALS IN STAGE I CARCINOMA OF THE ENDOMETRIUM

Author	Preoperative Irradiation plus Surgery		Surgery Alone		Irradiation Alone	
	No. of Patients	Per Cent Survival	No. of Patients	Per Cent Survival	No. of Patients	Per Cent Survival
Truskett and Constable[17]	82/100	82	43/55	78.1	10/10	52.6
Davis[3]	27/40	67.5	107/200	53.5		
Beck *et al.*[1]	108/152	71	158/186	85	98/192	51
Sala and del Regato[14]	45/57	79				
Robert[13]	25/31	80.6	84/103	82	5/10	50
Gusberg and Yannopoulos[5]	39/45	86.7	56/69	81.2		
Totals	326/425	77	448/613	73	113/221	51

have grouped all patients according to those variables correlating with prognosis, which we have found to be uterine size, patient age, and tumor histology. Thus grouped, they make up relatively homogeneous prognostic classes within the Stage I category.[7] Our system is designed to minimize variation in survival within the classes so that the only remaining major variable is the method of treatment.

CONCLUSIONS

Our data suggest the following conclusions: In young patients (defined as those less than 50 years old), who have relatively benign tumors (defined as histologic Grade 0 or 1), surgery alone appears to be the treatment of choice. This, in general agreement with Kempson and Pokorny,[6] recommends, in low grade lesions, a trial with progestational agents and curettage; if the lesion does not respond, a hysterectomy is advised.

In patients 50 to 69 years of age, with histologic Grade 0 tumors, surgery alone may also be the treatment of choice. Verification of the above statements will require further study with a larger group of patients.

In patients 50 to 69 years of age, independent of the uterine depth and with histologic Grades 1 through 3; in patients less than 50 years of age, with tumors of histologic Grades 2 or 3, and in patients 70 years of age or older with tumor Grades 0 or 1, the treatment of choice appears to be preoperative irradiation followed by surgery.

In patients over 70 years of age with histologic Grades 2 or 3 tumor, there is no clear-cut survival difference between treatment regimens. Further study with larger groups will be required to define optimal therapy in these patients. In this last group there was a significant rate of recurrence of tumor following surgery alone as well as a higher 5 year cancer mortality. The data thus suggest that, if feasible, preoperative irradiation followed by hysterectomy might be the treatment of choice. Irradiation alone would almost surely be the treatment of choice in patients unable to withstand surgery regardless of age.

In most patients intrauterine radium alone was used for irradiation. It is predicated that the addition of external irradiation would further improve survival. This should be especially true in histologic Grades 2 and 3.

SUMMARY

A series of 790 patients with Stage I carcinoma of the corpus uteri, collected from 1940 to 1963, was divided into sets of prognostically distinct groups. The groups were arranged according to the patients age and histologic grade of their tumor. The uterine depth of the patients was used as

well, where applicable. Within each group there was minimal variation in survival rates. The only major variable according to our data was therapy. Therefore, the relative merits of surgery and irradiation were readily comparable.

Our study suggests that hysterectomy combined with irradiation (preoperative) appears to be the treatment of choice in Stage I cancer of the endometrium, except in the young patients with low grade tumors where surgery alone may suffice. In patients unable to withstand surgery, irradiation alone appears to be the treatment of choice.

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MIXED MESODERMAL SARCOMA OF THE UTERUS*

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MIXED mesodermal sarcoma of the uterus is a relatively rare tumor that is associated with a grave prognosis. Sternberg *et al.*,[5] for instance, reported 21 cases, all succumbing to the disease. In 1966 Edwards[2] reported a 42 per cent 2 year survival in a selected group of patients who were treated at the M. D. Anderson Hospital and Tumor Institute at Houston, Texas with preoperative radium therapy followed by hysterectomy.

This paper enlarges on that report by analyzing the treatment techniques and results on all patients seen at our hospital with this diagnosis during the period from March 1944 through December 1969, including a recent group of patients treated with preoperative whole pelvis irradiation, radium insertion and hysterectomy.

CLINICAL MATERIAL

From March 1944 through December 1969, 101 patients with mixed mesodermal sarcoma of the uterus were seen at the M. D. Anderson Hospital. Follow-up information is available on 94 patients including 19 patients who in early years received no treatment because of far advanced disease. Thus, 75 patients are available for analysis of treatment techniques.

The age range of 31 to 85 years with an average of 59.9 years is comparable with other reported age incidences.[1,3,4,7] Seventy-five of the 94 patients were in the fifth, sixth, or seventh decades of life when the diagnosis was made, as shown in Figure 1.

Twelve per cent of the patients in our series were nulliparous, while 30 per cent were Negroid, suggesting a higher incidence than in Caucasians (Table 1).

Careful review of the history of the 94 patients revealed that none of the patients had received either pelvic irradiation or intracavitary radium prior to the diagnosis of mixed mesodermal sarcoma of the uterus; thus, preliminary irradiation is probably not significant in the etiology of this lesion.

The interval between the onset of symptoms and the diagnosis was relatively short, usually less than 5 months.

Postmenopausal bleeding was the dominant presenting symptom. Abdominal pain and distention were experienced by a very small percentage of the patients. Other complaints included watery vaginal discharge, anorexia with weight loss, dysuria, and/or edema.

The association of obesity, diabetes and hypertension in the patients with this

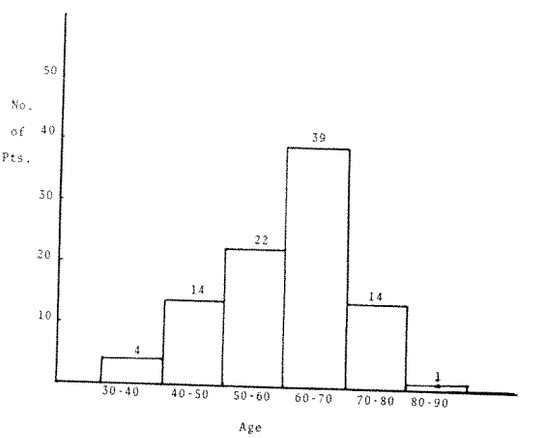


FIG. 1. Age distribution.

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malignancy was high (Table I). Thirty-eight patients (40 per cent) were diabetic at the time of diagnosis, 43 patients (45 per cent) had a diagnosis of obesity, and hypertension was seen in 23 patients for an incidence of 24 per cent of the total group.

CLINICAL GROUPING

Since the extent of disease is usually of prognostic significance in gynecologic malignancies, a clinical-surgical classification was established as follows:

Group I: Disease confined to corpus uteri.

Group II: Extension to cervix, vagina and/or parametrium.

Group III: Extension outside pelvis.

Physical examination, radiographic findings and/or surgical findings were utilized in this classification scheme; unfortunately, depth of myometrial invasion was not sufficiently frequently recorded to be of consistent value.

TREATMENT TECHNIQUES

Various treatment modalities and combinations thereof have been used in the treatment of these patients including: (1) hysterectomy alone; (2) hysterectomy followed by postoperative external irradiation; (3) preoperative radium followed by hysterectomy; and (4) irradiation alone where surgery was refused or contraindicated because of the extent of disease or medical problems. Recently (1966–1969) most patients received external irradiation plus radium preoperatively in an attempt to give a more homogeneous dose to uterus and pelvic lymphatics. In earlier years, 19 patients were not treated, mostly because of advanced disease, although a few refused treatment.

TABLE I

Parity	No. of Patients
Nulligravida	11
Multigravida	80
Race	
Caucasian	66 (70%)
Negro	28 (30%)
Associated Diseases	
Diabetes	38 (40%)
Hypertension	23 (24%)
Obesity	43 (45%)

TABLE II

LENGTH OF SURVIVAL OF PATIENTS DEAD WITH DISEASE

	Months			
No. of Patients	0–12	12–24	24–36	>36
	50	11	4	4

73 per cent dead within 12 months of diagnosis.
88 per cent dead within 24 months of diagnosis

When preoperative radium was utilized, 5,000 mg.-hours of radium were given in 2 insertions of Heyman capsules and intrauterine tandem plus 7,000–8,000 rads vaginal mucosal dose from Fletcher colpostats. The radium insertions were separated by 2 weeks. When external irradiation was utilized, whole pelvis irradiation of 4,000 rads in 4 weeks with the 22 mev. betatron photon beam was delivered through anteroposterior-posteroanterior 15×15 cm. portals, followed by a Heyman capsule intrauterine packing to deliver 2,500 mg.-hours. Afterloading Fletcher colpostats were also inserted to deliver 4,000 rads mucosal dose to the upper vagina. Hysterectomy and bilateral salpingo-oophorectomy followed the preoperative radium (or external irradiation) in 4–6 weeks.

RESULTS

The results are shown in Tables II–VI according to extent of disease and treatment modalities. The 24 month NED (no evidence of disease) rate is valid for analysis of treatment techniques since almost all recurrences or distant metastases occur within that time period (Table II).

Survival is directly related to the extent of disease as shown in Table III. Those patients with tumor confined to the corpus have a good chance of local control (68 per cent) and survival (53 per cent), although

TABLE III

OVER-ALL RESULTS BY EXTENT OF DISEASE

Extent of Disease	No. of Patients	NED (2 years)	Local Control (Pelvis)
Group I Corpus Alone	34	18/34 (53%)	23/34 (68%)
Group II Cervix, Vagina and/or Parametrium	35	3/35 (8.5%)	10/35 (29%)
Group III Outside Pelvis	25	0/25 (0%)	5/25 (20%)

NED = No evidence of disease.

some patients are lost because of upper abdominal disease or distant metastases. Extension of disease outside the corpus markedly lessens the outlook (Table III).

Analysis of the results as related to the various treatment modalities is made more difficult by the necessity of correlating the results with the extent of disease. The previous report by Edwards[2] indicated improved results when preoperative radium was utilized rather than hysterectomy alone. However, most of these patients had limited disease and, in fact, in Group I, it is difficult to show an advantage of one modality over another with the exception that some combination of surgery and radium appears preferable to either hysterectomy alone or irradiation alone (Tables IV, V, and VI).

Table VII compares the local control and survival in Groups I and II between patients who have been treated with hysterectomy or irradiation alone, in contrast to those receiving preoperative radium or external irradiation followed by hysterectomy. Patients with microscopic disease found incidentally at hysterectomy who received postoperative irradiation are not included. A statistically significant difference is not shown between preoperative radium and external irradiation. Both show an excellent rate of pelvic control, and markedly improved results over irradiation or hysterectomy alone.

DISCUSSION

The term mixed mesodermal sarcoma is appropriate because it gives some indication of the nature of the tumor, and bears relation to a similar type of tumor occurring in other organs. There appears to be no benefit in further subdividing these tumors

TABLE IV

TREATMENT PLANS IN GROUP I WITH RESULTS

Treatment	No. of Patients	NED (2 years)	Local Control
Hysterectomy Alone	5	2	2
Hysterectomy + Postoperative Irradiation	7	4	5
Preoperative Radium + Hysterectomy	12	7	10
Preoperative Irradiation + Radium + Hysterectomy	5	3	4
Irradiation Only	5	2	2
Total	34	18 (53%)	23 (70%)

TABLE V

TREATMENT PLANS IN GROUP II WITH RESULTS

Treatment	No. of Patients	NED (2 years)	Local Control
Hysterectomy Alone	5	0	0
Hysterectomy + Postoperative Irradiation	5	1	4
Preoperative Radium + Hysterectomy	1	1	1
Preoperative Irradiation + Radium + Hysterectomy	5	1	5
Irradiation Only	6	0	0
Incomplete Treatment	13	0	0
Total	35	3	10

histologically since the prognosis is similar for the entire group with the possible exception of the pure homologous type known as endometrial stromal sarcoma.

There are various theories of origin of these tumors,[2,5] but probably they arise from the epithelial stroma of the endometrium, cervix or upper vagina, occurring in children as sarcoma botryoides or in adults as mixed mesodermal sarcoma of the endometrium. The tumor tissue appears primitive and its pluripotential capabilities may explain the diversity of the histologic picture. Although the epithelial components in these tumors are limited to those of the female genital system, this is certainly not true of the sarcomatous elements. Supporting the argument of the origin from epithelial stroma is the observation that these tumors characteristically arise in epithelial areas, never deep within the organ.

These growths may be silent for some time with gradual enlargement until they present as a pedunculated growth extending through the os into the vagina. Concomitant with the growth of this neoplasm to involve the cervix and vagina is a progressive distention of the endometrial cavity and invasion of the myometrium.

Many of our patients have had pelvic control of tumor through combined irradiation and hysterectomy only to recur with disease in the upper abdomen. Distant

TABLE VI

TREATMENT PLANS IN GROUP III WITH RESULTS

Treatment	No. of Patients	NED (2 years)	Local Control
Hysterectomy Alone	5	0	2
Hysterectomy + Postoperative Irradiation	4	0	1
Preoperative Radium + Hysterectomy	1	0	1
Preoperative Irradiation + Radium + Hysterectomy	2	0	1
Irradiation Only	7	0	0
Incomplete Treatment	6	0	0
Total	25	0	5

TABLE VII

SURVIVAL AND LOCAL CONTROL BY TREATMENT MODALITIES

(Groups I and II only)

	NED	Pelvic Control
Hysterectomy Alone	2/10	2/10
External Irradiation Alone	2/11	2/11
Preoperative Radium and Hysterectomy	8/13	11/13
Preoperative External Irradiation, Radium and Hysterectomy	4/10	9/10

metastases can also occur, although the usual mechanism of death is intraabdominal disease. Indeed pulmonary metastases were seen by chest roentgenograms and/or autopsy in only 14 of the 94 patients (15 per cent).

We have previously suggested the value of preoperative radium prior to hysterectomy in selected patients.[2] More recently, on theoretical grounds, it seemed logical to deliver a more homogeneous dose of external irradiation to the primary tumor and pelvic lymphatics followed by Heyman packing and/or intrauterine tandem insertion with vaginal radium. A hysterectomy and bilateral salpingo-oophorectomy was done 6 weeks later. Although the results when correlated with the extent of disease do not show any statistically significant advantage of this mode of therapy over preoperative radium plus hysterectomy, it is our distinct clinical impression that the latter group treated with external irradiation have generally been patients with more extensive disease and larger uteri than those treated prior to 1965 by preoperative radium and hysterectomy. In recent years these patients with large uteri who have been treated using external radiotherapy, radium and hysterectomy technique have had an improved rate of local control (65–75 per cent in Groups I and II). Further improvement in survival rates might result from combination of irradiation and surgery with chemotherapy.

Patients in whom microscopic disease is discovered incidentally at the time of hysterectomy who receive postoperative irradiation have an excellent outlook, but the good results are chiefly related to the limited extent of disease rather than to the efficacy of the treatment modality.

CONCLUSIONS

1. Mixed mesodermal sarcoma of the uterus remains a devastating disease with a guarded prognosis.
2. Both local control and survival are chiefly related to the extent of disease.
3. The combination of irradiation and hysterectomy appears to be superior to either irradiation or hysterectomy alone.
4. External irradiation, single Heyman packing followed by hysterectomy and bilateral salpingo-oophorectomy offer the best chance of local pelvic control of the tumor and long-term survival.

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CHORIOCARCINOMA*

ASPECTS OF THE CLINICAL PATHOLOGY

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CHORIOCARCINOMA is an unusual neoplasm. It arises most commonly from the trophoblast. It secretes a hormone, human chorionic gonadotrophin (HCG), and can disappear spontaneously despite distant metastatic disease. It was the first, and is still the only malignant neoplasm generally accepted as curable after systemic spread has occurred. It can mimic almost every disease in the female and thus be diagnostically most deceptive. It is commonly first diagnosed by biopsy of a metastasis, the primary lesion often remaining silent. It differs from many other neoplasms in the rapidity of growth and its frequently hemorrhagic character. All too often, the diagnosis is made post mortem.

The following case illustrates the multiple problems characteristic of this disease.

REPORT OF A CASE

A 27 year old woman entered the hospital with the chief complaint of hemoptysis, increasing dyspnea and chest pain of 1 day's duration. The onset of her present illness is difficult to identify, but is probably *not* related to her first pregnancy 3 years prior to this admission, at which time she delivered a full-term child under local anesthesia with spontaneous delivery of the placenta. Her pregnancy had been uncomplicated except for a short episode of hyperemesis gravidarum for which she was hospitalized in her third month of pregnancy. Her present illness could be dated to her second pregnancy 2 years prior to this admission. Her pregnancy ended in a full-term spontaneous delivery at home. The patient was admitted to the hospital and the placenta was expelled in the hospital.

Eleven months later the patient was readmitted for dysfunctional uterine bleeding. Dilatation and curettage were performed. The pathologic report was endometrial dystrophy.

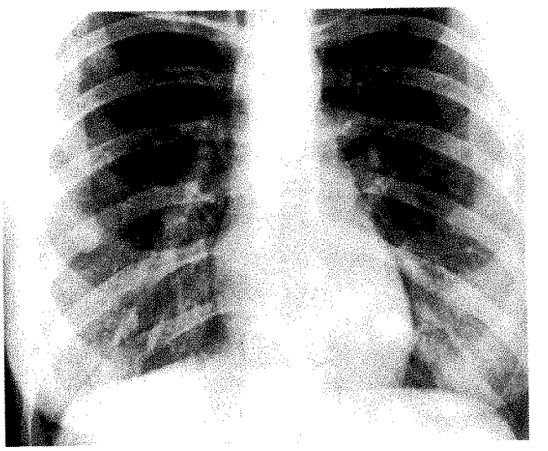


FIG. 1. Frontal chest roentgenogram showing minimal increased lucency of the right upper lobe.

The patient did well and she was discharged shortly after the dilatation and curettage.

Ten days later, the patient was admitted with right-sided chest pain, acute in onset, pleuritic in nature; however, no hemoptysis or sputum production was present. A chest roentgenogram at this time showed very minimal increased lucency of the right upper lobe (Fig. 1). More detailed questions elicited a history of 1 year of intermittent episodes of right-sided chest pain starting shortly after her second pregnancy. Lung scanning at this time revealed perfusion defects in the right upper and lower lobes (Fig. 2; and 3). Six days later, pulmonary angiography revealed a definite pulmonary embolus in the right upper lobe obstructing the arterial circulation (Fig. 4). Anticoagulation was started. The chest pain persisted for 4 days and gradually subsided. Six days after the onset of anticoagulation, the patient was discharged in good condition.

Two months after the lung scanning and the onset of anticoagulation, the patient entered the hospital once again with an acute episode of chest pain of 12 hours' duration. Detailed history suggested that in the interim 2 months

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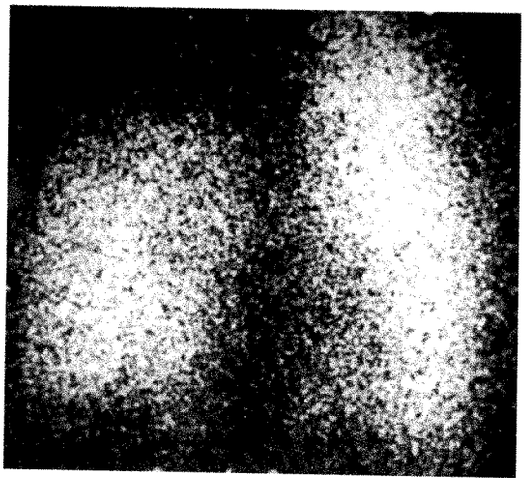


Fig. 2. Lung scan, anterior position, reveals perfusion defects in the right upper and lower lobes.

between the onset of anticoagulation and the admission, at least 12 episodes of probable pulmonary emboli had occurred with accompanying right chest pain. At this time, it was felt that laparotomy should be performed to evaluate the possibility of emboli originating from thrombus in the uterus, ovarian veins, and possibly vena cava. One day after admission, hysterectomy and a total abdominal salpingo-oophorectomy were performed. At operation, the right side of the uterus and the broad ligament contained 4 to 5 distended veins. It was felt that this could be a source of emboli. The vena cava was explored and no clot was demonstrated. Pathologic examination of the surgical specimen revealed a proliferative endometrium. No clot or tumor was demonstrated. Six days after operation while anticoagulated, she experienced sudden left chest pain which slowly improved over the next few days. Ap-

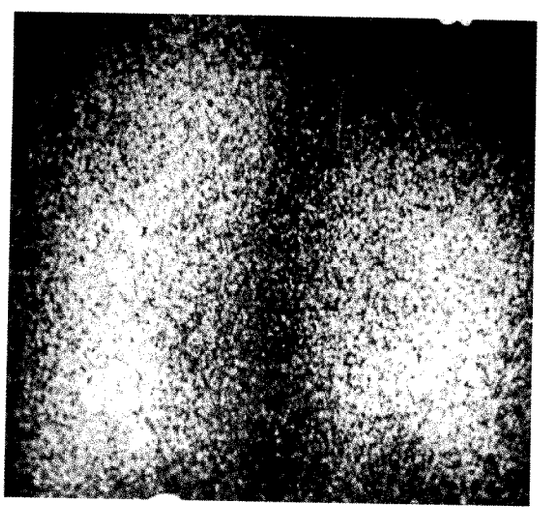


Fig. 3. Lung scan, posterior position, shows defects in the right upper and lower lobes.

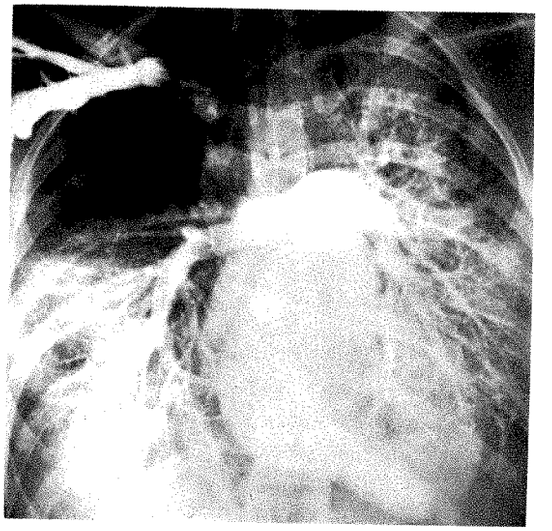


Fig. 4. Pulmonary angiogram reveals a pulmonary embolus obstructing the right upper lobe arterial supply.



Fig. 5. Venogram of both lower legs is normal.

proximately 10 days postoperative, the patient was again discharged on anticoagulants.

The patient did well for 2 months and then presented with the chief complaint of hemoptysis, dyspnea and chest pain of 1 day's duration. This was despite anticoagulation with a maintained prothrombin time of 2 to 3 times normal. In the preceding 2 weeks, there had been 3 definite episodes of chest pain, 1 on the left and 2 on the right, with the episode just prior to this admission being the fourth episode. The patient had experienced in these 2 months increasing dyspnea with difficulty in exercising to the point of being unable to ride her bicycle.

She was admitted to the hospital at this time because of her generally deteriorated state and for possible inferior vena cava ligation. Venograms of both legs failed to reveal a source of emboli (Fig. 5; and 6). An inferior vena cavagram demonstrated total occlusion of the vena cava with collateralization around the vena cava suggesting a large amount of thrombus (Fig. 7). The iliac veins were also diffusely involved (Fig. 8). A repeat pulmonary angiogram showed a marked progression of the embolus in the right main pulmonary artery (Fig. 9). The thrombus, in addition to completely occluding the artery to the right upper lobe, had extended to partly occlude the pulmonary artery to the middle and lower lobes. The patient was taken to the operating room and a right pulmonary embolectomy, ligation of bilateral ovarian veins and clipping of the inferior vena cava were done. Clot was cleaned from the vena cava and iliac veins. Pathologic examination of the blood clots from the right pulmonary artery showed metastatic choriocarcinoma. No pathology was found in the ovarian veins. Twenty-four hour

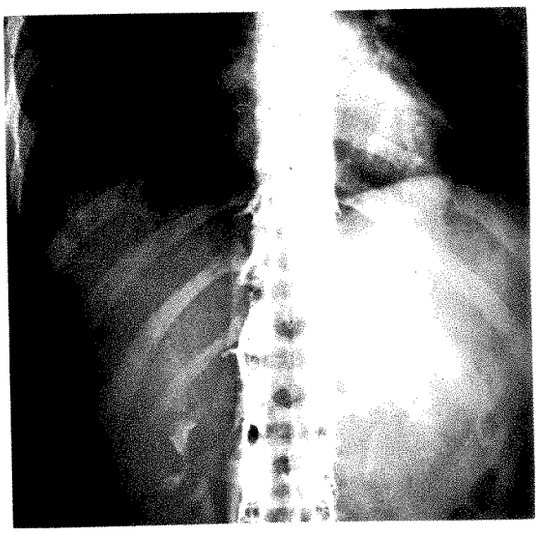


Fig. 7. An inferior vena cavagram demonstrates total occlusion of the vena cava with collateralization around the vena cava suggesting a large amount of thrombus.



Fig. 6. Venogram of both upper legs is normal.



Fig. 8. The iliac veins show occlusion with collateralization.



FIG. 9. A repeat pulmonary angiogram shows a marked progression of the embolus in the right main pulmonary artery. The thrombus, in addition to completely occluding the artery to the right upper lobe, has extended to partly occlude the pulmonary artery to the middle and lower lobes.

urine gonadotrophin assays were markedly elevated.

Chemotherapy was started consisting of 500 micrograms of actinomycin D intravenously for 5 days and 100 milligrams 6 mercaptopurine orally for 5 days. Gonadotrophin assays dropped markedly. One week later, a second course of therapy was again given. The patient was then discharged following stabilization. Eight weeks later, the patient was admitted for a third course of therapy. Since that time, the patient has done well. Prognosis is excellent.

DISCUSSION

Because of the younger age group, the diagnosis of malignancy is often not entertained as a possibility. It should be emphasized that unexpected, unusual, bizarre illness in a woman of reproductive age should always be regarded as possibly due to choriocarcinoma. Because of rapid growth rate and hemorrhagic tendency, it can produce an illness of relatively short duration and sudden onset.

The exact form of clinical presentation depends on location and behavior of the metastatic foci.[1,10] Intracranial hemorrhage is a much commoner first sign of disease than reports would suggest.[7,25,29] Visual disturbances due to choroidal metastases have been reported in many instances.[3] Other ocular metastatic diseases may be reported as well.[26,30] Epistaxis is not uncommon and can be fatal.[9] Pleural effusion has been reported as the first sign of disease as late as 2 years after a normal pregnancy: this was associated with a choriocarcinomatous mass in the left lung.[2] Cardiorespiratory disturbances have long been recognized as the cause of death in patients with multiple pulmonary involvement.[11] More subtly, however, diffuse showers of intra-arterial occlusive emboli by choriocarcinoma with associated thrombus may present as central pulmonary hypertension with cor pulmonale. Even at this point, the disease may be curable. Reports of this general problem have been numerous in the last several years.[4,5,6,15] Dyspnea in patients with terminal neoplastic disease from choriocarcinoma on the basis of massive pulmonary replacement is common. In a series of 92 patients with choriocarcinoma, 22 instances occurred of severe terminal dyspnea.[16] An occasional patient will present with a picture of diffuse choriocarcinoma with dyspnea with a normal pregnancy in the immediate past or several years prior to the terminal problem. The diagnosis of intra-arterial pulmonary choriocarcinoma with a normal uterus has been made after death. Abdominal disturbances of various kinds have been reported. Hepatic metastases and symptomatology suggesting acute cholecystitis have been seen.[14,31] Jaundice and intraperitoneal hemorrhage have been described. Jaundice appears to be almost always a terminal finding due to metastatic involvement of the liver.[8] Intraperitoneal hemorrhage has occurred from spleen, liver and uterus. Intestinal hemorrhage[12] and intussusception have occurred secondary to metastatic involvement of the small bowel.[22]

Choriocarcinoma may occur abnormally in place and time. It can be considered acting classically, if it occurs in the body of the uterus during reproductive life and

produces diagnostic signs and symptoms within, at most, 2 years of a certain or probable pregnancy. It can, however, differ not uncommonly from the classical pattern. It can occur in the vulva, vagina, cervix, tubes, ovaries and even the broad ligament and peritoneal cavity.[23,24,28] Extragenital choriocarcinoma can occur not uncommonly; *i.e.*, a patient with widespread metastatic choriocarcinoma is found at hysterectomy or after death to have a normal uterus and no reasonably possible primary lesion at a gestational site. The patient may be known to have had or be only suspected of having had a possible causative pregnancy. Serial sections of many uteri have removed doubt that absence of demonstrable primary lesion is a fact. This very confusing aspect of the disease was first described by Teacher in 1903[27] and is more common than generally thought.[17,18,21] In some series, one-third of patients dead of choriocarcinoma showed no demonstrable primary lesion in the uterus.

The lesion may appear 2 years or more after certain or probable pregnancy. On the grounds of timing, it appears unrelated to the previous pregnancy. It can appear after menopause which is perhaps even more troubling. Another more complicated situation is where a choriocarcinoma develops after a normal pregnancy in a patient who has had a hydatidiform mole on an earlier occasion. This again is a long recognized and well documented occurrence.[19] The diagnosis of choriocarcinoma today is probably made at least as often without histologic proof as with it. Active, persisting trophoblast can be detected and eradicated with the location of the primary lesion remaining unknown.

Lastly, the etiology of choriocarcinoma remains unknown. One of the more modern concepts which seems to hold out promise is the postulation of immunologic balance between fetus and mother.

SUMMARY

An unexpected, unusual, bizarre illness in a woman of reproductive age should always be regarded as possibly due to choriocarcinoma. If the disease is diagnosed by biopsy of a metastasis, the pathology is suggested.

Presentation in the form of hemorrhage or cardiorespiratory disturbances is common.

It is still the only tumor generally accepted as curable after diffuse metastases have occurred. Herein lies the immediacy of the problem; *i.e.*, a disease that is capable of rapid involvement of the body by metastases, causing typically severe complications such as intracranial hemorrhage and pulmonary emboli, can, even in this catastrophic, severely advanced stage, be completely reversible if diagnosed in time.

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SEMINOMA OF THE TESTIS*

By VIRENDRA S. SAXENA, B.Sc., M.D., D.M.R.T., F.F.R. (ENGLAND)†

DURING the period of 1947 to 1969, 207 patients with malignant testicular tumors were registered at Brooke General Hospital (B.G.H.), Fort Sam Houston, Texas. Of these, 77 patients had histologically proven pure seminoma of their testes (Table 1). Two of these patients with seminoma were managed primarily outside of this hospital, and were seen here only for their follow-up examinations for any evidence of recurrence of their disease. These 2 cases have been excluded from this study. This makes a total determinate number of 75 cases that are available for this study.

AGE INCIDENCE

Most of our patients were between the ages of 21 years and 40 years with the highest number in the third decade of their life (Fig. 1).

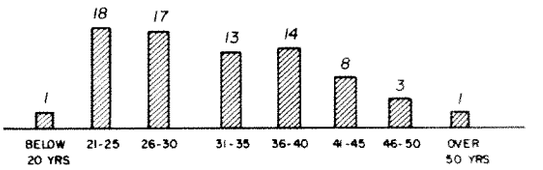


FIG. 1. Age incidence.

SIDE OF INVOLVEMENT

The right and left testis was involved with almost equal frequency, the left one a little more commonly than the right. Thus there were 40 patients who had involvement of their left testis as compared to 35 patients with right-sided involvement (Fig. 2).

DIAGNOSIS

All of these patients had simple orchiectomy with a high ligation of their spermatic cord for the purposes of establishing a diagnosis. The spermatic cord would be exposed first within the inguinal canal before it would be clamped, ligated, and divided at the level of the internal inguinal ring. The testicle would then be delivered through this incision from the scrotum.

TABLE I

TOTAL NUMBER OF PATIENTS WITH SEMINOMA OF TESTIS

Seen at B.G.H. (1947–1969)	77
No. of patients treated elsewhere	2
Determinate No. of patients	75

B.G.H. = Brooke General Hospital.

PATHOLOGY

The excised testes along with the spermatic cord on all these patients were examined at the Pathology Service of the Brooke General Hospital, Fort Sam Houston, Texas. Multiple sections through different parts of the excised testes and the spermatic cord containing normal and tumor tissue were obtained and studied by the senior pathologists. In those cases where any doubt existed as to the exact diagnosis, the tissues from their tumors were then examined by the pathologists at the Armed Forces Institute of Pathology, Washington, D. C.

Microscopic study of the diseased testes in all these patients showed a remarkable picture of uniformity in the appearance of the cell structure and their arrangement. It showed cords of round or polygonal cells, each cord containing anywhere from 4 to 10 cells. The cytoplasmic boundaries

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The above study was done while the author was Chief, Radiotherapy Section, Department of Radiology at Brooke General Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas from 1969–1971.

The opinions contained in this study are strictly those of the author and not of the Office of the Surgeon General, Department of the Army, or of any individual now serving in the United States Army.

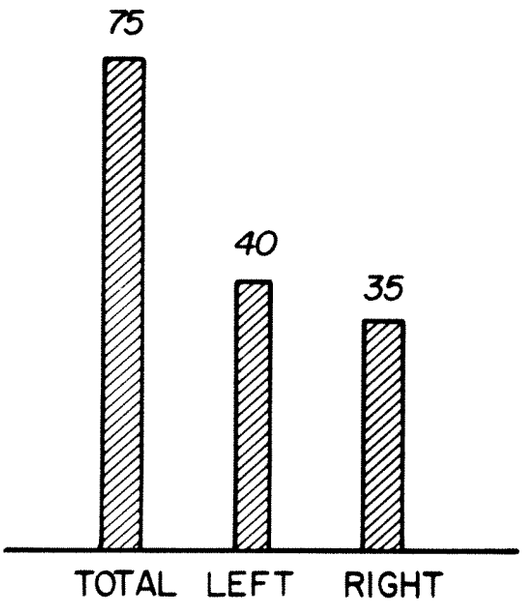


Fig. 2. Side of involvement.

of these cells were hard to distinguish. These cells had clear cytoplasm. The nuclei were enlarged and were round to oval.

Of 75 patients there were only 4 instances, where there was invasion of the spermatic cord by the tumor at the time of orchiectomy.

CLINICAL STAGING

The purpose of clinical staging in testicular tumors is mainly to plan treatment and to evaluate the efficacy of this treatment. The accuracy of clinical staging depends largely on the level of refinements in our investigative systems to detect an early spread of the disease beyond the primary site of origin of the seminoma.

In testicular tumors the main and earliest routes of spread are to the retroperitoneal lymphatics in the abdomen at the level of renal veins; the other areas of metastatic spread in the abdomen are the internal iliac lymph nodes on both sides by retrograde spread from the periaortic lymph nodes. The inguinal lymph nodes may also be involved, if the patient had previous surgery through the scrotal skin; for example, herniorrhaphy, biopsy, or orchidopexy. In advanced cases the patients may have disease already spreading to the mediastinum, supraclavicular lymph nodes, mostly on the left side, and the lungs.

The clinical staging used in this study is as follows (Fig. 3):

Stage I Tumor strictly confined to testis and spermatic cord

Stage II Demonstrable metastatic disease outside the testis and spermatic cord, into the abdomen but below the diaphragm

Stage III Wide spread metastasis

A. Confined to lymphatic system; for example, the mediastinum and the supraclavicular areas

B. Extranodal involvement; for example, the abdominal viscera or distant metastasis.

In this study the patients were staged by physical examination, chest roentgenography, intravenous pyelography, and more recently by pedal lymphangiography—following simple orchiectomy. A small number of the patients in the past had abdominal exploration and an attempt was made to do retroperitoneal lymphadenectomy. Pedal lymphangiography has recently become a routine procedure in patients with testicular tumors. When a lymphangiogram shows enlargement, and/or blockage of the lymphatics, its value is significant, especially if correlated with other investigative and clinical findings, in

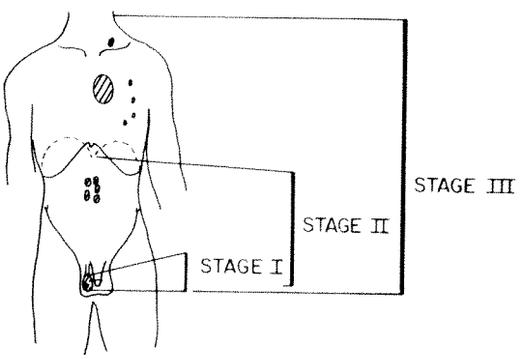


Fig. 3. Clinical staging.

staging the disease. However, a negative pedal lymphangiogram does not exclude the presence of abdominal spread. A 24 year old white male was transferred to this institution in 1969 from one of our army bases in Japan, having had an orchiectomy performed on his left side there. The histologic diagnosis was pure seminoma. On routine investigation it was found that the patient's left ureter was partially obstructed by the presence of a mass in the left lower quadrant of the abdomen as can be seen in Figure 4. Pedal lymphangiograms obtained on him were reported as normal (Fig. 5, *A* and *B*).

In this study all but 2 patients had Stage I seminoma of the testis. The 2 patients had Stage II disease (Fig. 6).

TREATMENT POLICIES

In this series, there were 3 main methods of managing the patients with seminoma of the testis following simple orchiectomy (Table II):

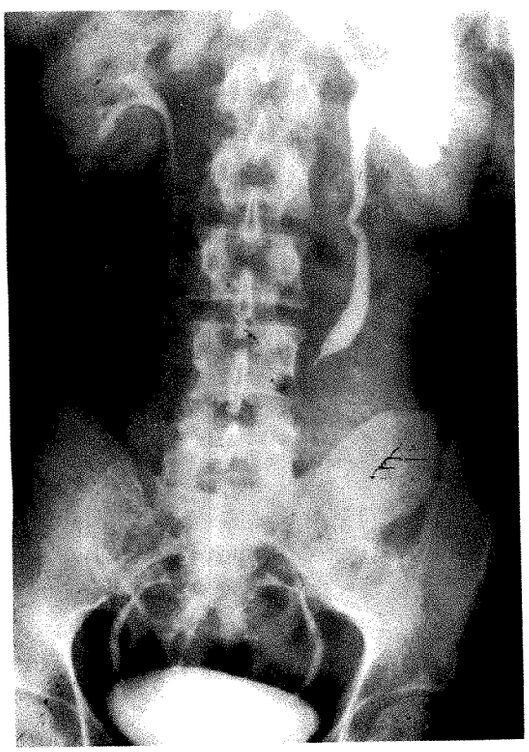


FIG. 4. Partial obstruction of the left ureter by a mass in the left lower quadrant of the abdomen.

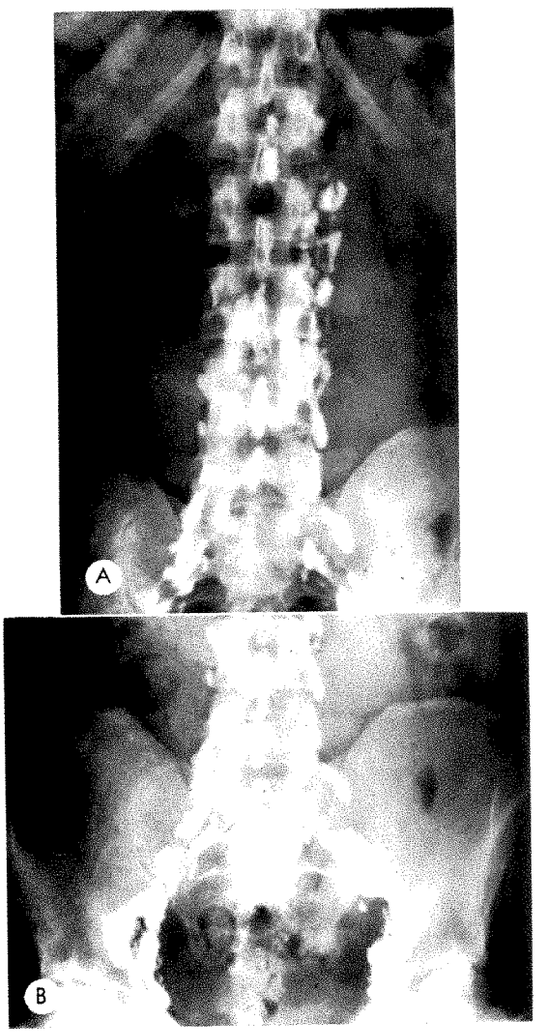


FIG. 5. (*A* and *B*) Pedal lymphangiograms reported as normal.

1. Retroperitoneal lymphadenectomy with either pre- or postoperative inguinal and abdominal paraaortic nodal irradiation
2. Irradiation only to the inguinal and abdominal paraaortic lymphatics
3. Irradiation only to the inguinal, abdominal, paraaortic, mediastinal, and supraclavicular lymphatics, called extended nodal irradiation here.

RETROPERITONEAL LYMPHADENECTOMY—PRINCIPLES OF THE TECHNIQUE

During the earlier years of this series the patients with seminoma of the testis were

TABLE II

IRRADIATION POLICIES OF SEMINOMA OF TESTIS

Paraaortic lymphadenectomy+extended nodal irradiation	1
Paraaortic lymphadenectomy+abdominal nodal irradiation	10
Irradiation only to inguinal and abdominal paraaortic lymph nodes	11
Extended nodal irradiation only	53
Total	75

subjected routinely to abdominal retroperitoneal lymphadenectomy followed by postoperative irradiation to the inguinal and abdominal paraaortic lymphatics up to the attachment.

The retroperitoneal lymphadenectomy was done under spinal anesthesia. The skin incision extended from the tip of the 11th rib downward, about 4 cm. medial, to the anterosuperior iliac spine reaching Poupart's ligament at about its midpoint and then swinging in an arc to the external inguinal ring. The external oblique fascia was first opened in the inferior angle of the wound. The spermatic cord was identified and the stump pulled out of the scrotum and detached. The cord was freed to the point of the internal inguinal ring. Attention was then directed to the superior angle of the wound. After exposing all the abdominal muscles and fascia, an incision was made through them corresponding to the length of the skin wound. The peritoneum was exposed and carefully reflected anteriorly towards the midline without opening it. The dissection began by freeing the spermatic cord from the bed, and moving upward, dissecting, *en bloc* all the midline tissues containing the lymph nodes in the pelvis and the paraaortic region. One Penrose drain was placed down to one side of the bladder and another at the inferior pole of the ipsilateral kidney. The wound was closed in layers in the usual manner.

IRRADIATION TECHNIQUE

In earlier years orthovoltage was used in treating these patients. The unit was operated at 220 kvp., and 15 ma. It pro roentgen rays of 1.25 mm. Cu HVL a added filtration of 0.5 mm. Cu and Al. A midline dose of 2,000–3,000 delivered at a rate of 200 r per trea per day. All but 1 of these patie ceived irradiation to the inguina paraaortic lymph nodes only.

At later periods the retroperi lymphadenectomy was abandoned in of irradiation only following a orchiectomy. The irradiation facto mained the same as described abov in this group of patients not only t guinal and abdominal paraaortic phatics were irradiated, but the irrad volume was extended to the medias and the left supraclavicular lymph The details of these ports are sho Figure 7.

More recently, the technique an volume of irradiation in Stage 1 semi of the testis has been altered. Cob teletherapy units are now used in irr ing these patients. The volume of high irradiation includes the inguinal lym ics, the empty scrotum on the ipsil side and the paraaortic lymph nodes the crura of the diaphragm. The rest area, including the normal testis is sh by lead blocks of appropriate thic Posteriorly, the irradiation port ex from the crura of the diaphragm t upper ⅓rd of the sacrum. The deta the port arrangement are shown in F 8. In order to treat this volume w

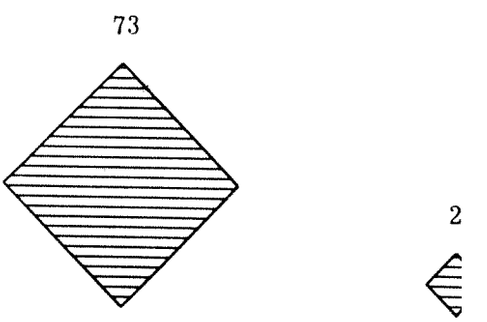


FIG. 6. Incidence of clinical staging.

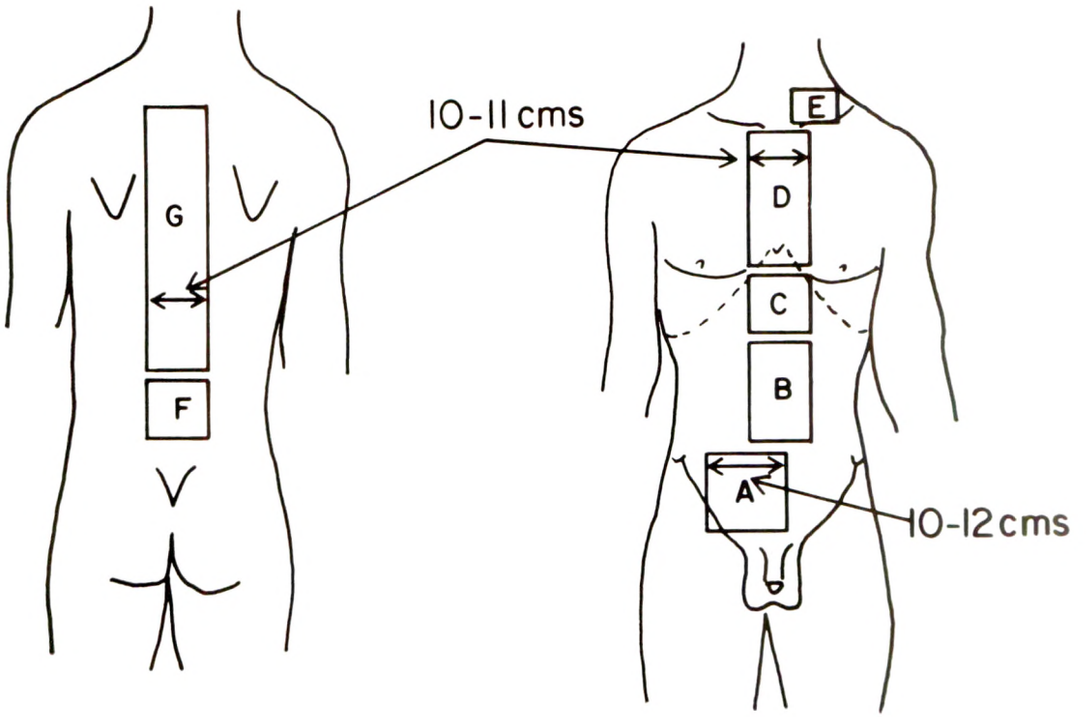


Fig. 7. Extended irradiation of lymph nodes.

single port the source to skin distance must be 80 to 100 cm. A midline dose of 3,000 rads is delivered in 15 treatments and 3 weeks, exposing anterior and posterior ports on alternate days.

In patients with Stage II seminoma of the testis the volume of high dose will include the whole pelvis and the abdominal paraaortic lymphatics. A total midline dose of 3,000 rads is delivered to the inguinal and abdominal paraaortic lymphatics in 3 weeks and 15 treatments. A booster dose of 500 rads to 1,000 rads is added to the bulkier tumor mass. A "prophylactic" dose of 2,000 rads is given to the mediastinum and left supraclavicular lymph nodes routinely in patients with Stage II disease.

Thus, out of 75 patients with pure seminoma of the testis, 53 received radiation therapy only to the ipsilateral inguinal, abdominal paraaortic, mediastinal, and the left supraclavicular lymphatics (Table II). All but 1 of these patients had Stage I seminoma of the testis. The one patient mentioned above had Stage II disease. There were 11 patients who had retroperitoneal lymphadenectomy with either preoperative or postoperative irradiation to the ipsilateral inguinal, and abdominal paraaortic lymphatics only. There were 6 patients who received postoperative irradiation. In none of this group of patients did the surgical specimen show any microscopic evidence of metastatic spread into the lymph nodes. Only one patient out of these 11 patients had extended nodal irradiation up to the left supraclavicular fossa, following retroperitoneal lymphadenectomy.

A total of 11 patients with Stage I disease had irradiation alone following simple orchiectomy to the ipsilateral inguinal, and abdominal paraaortic lymphatics only.

RESULTS

Some of these patients have been followed for as long as 20 years; the minimum length of follow-up in this study was 2

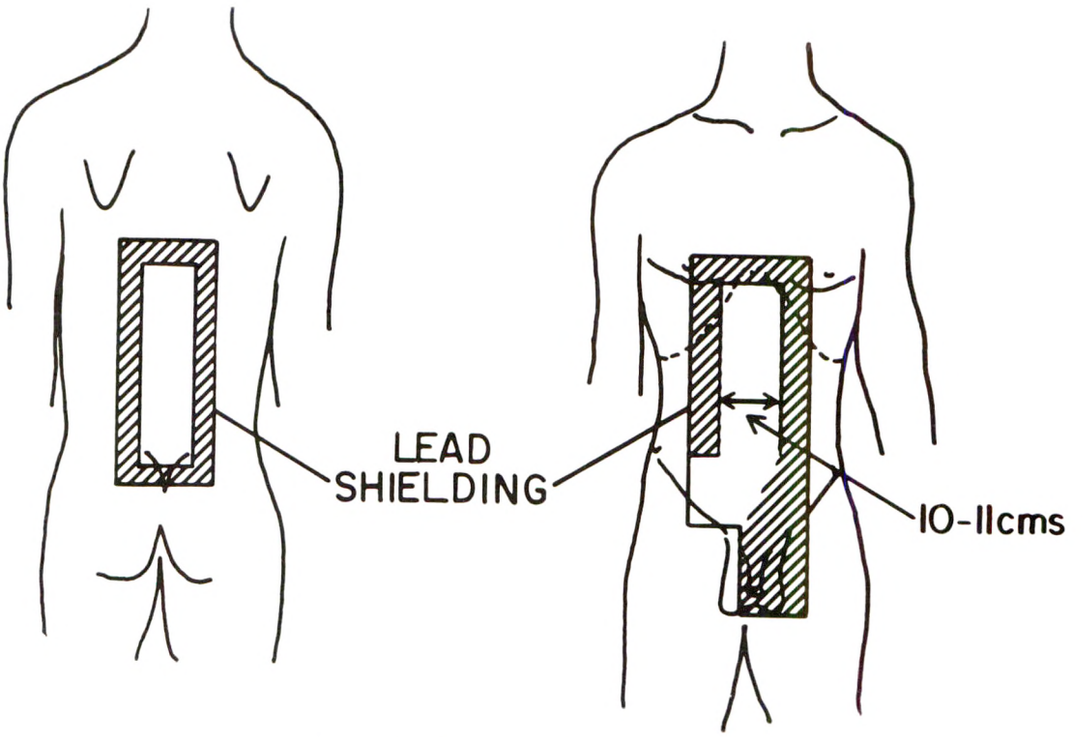


Fig. 8. Inguinal and paraaortic irradiation.

years. There are some patients who during these 20 years have lost all communication with the hospital Tumor Registry and are regarded as lost to follow-up. These patients are not necessarily dead. There are also some patients in this series who died of causes other than of seminoma of the testis. Therefore, to arrive at a fair conclusion of their survival rates, criteria for survival results have been established as shown in Table III. The exact number of patients lost to follow-up during the period of study is shown in Figure 9. Similarly all the patients who have died of extraneous causes are shown in Table IV.

Table III

CRITERIA FOR SURVIVAL

Dead of Seminoma
All patients lost to follow-up within 5 years
All patients dead of extraneous causes within 5 years
Patients Excluded
All patients either lost to follow-up or dead of extraneous causes after 5 years
Rest Included in Study

SURVIVAL RATES

The survival rates of all patients are shown in Table V. It is interesting to note

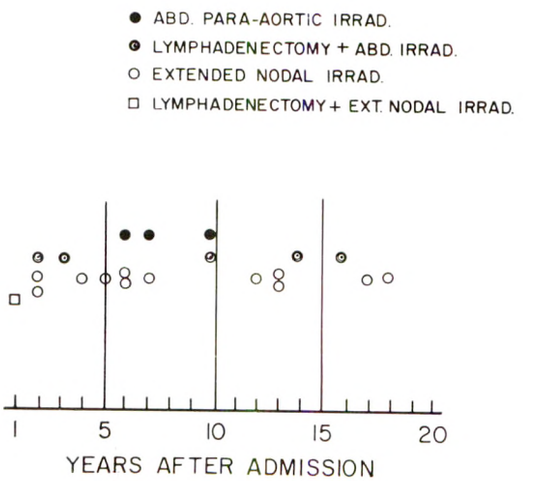


Fig. 9. Patients lost to follow-up.

TABLE IV

DEATHS FROM EXTRANEOUS CAUSES

Fifth year	1—Poisoning 1—Myocardial infarction
Sixth year	1—Malignant melanoma
Thirteenth year	1—Bombing attack
Total	4

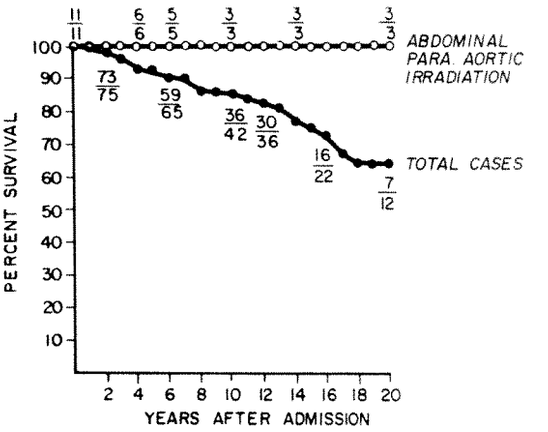


FIG. 10. Per cent of survival.

that no patient in this series died of seminoma as far as one could find out from the follow-up information. There were 7 patients out of 75 patients who were lost to follow-up in the first 5 years of this study (Fig. 9). They are all presumed to have died of their seminoma of the testis for the purpose of computing the survival rates. There were 4 patients who died of extraneous causes (Table IV).

The survival rates of all patients are shown in Table V and Figures 10 through 13. Thus we see that at the end of 3, 5, 7, 10, 15, and 20 years the survival rates are 96, 93, 90, 86, 75, and 59 per cent, respectively. These results are in agreement with the results reported by other authors.[1-5] In analyzing the results of the retroperitoneal lymphadenectomy with pre- or postoperative irradiation to the abdominal paraaortic lymphatics, one notes that the results are again quite comparable to those of other groups. There were 8 out of 10 patients at the end of 10 years and 5 out of 7 patients at the end of 15 years still alive and well without any evidence of disease (Fig. 10).

Maier *et al.*[4,5] have shown conclusively that the addition of retroperitoneal lymphadenectomy following orchiectomy with pre- or postoperative irradiation does not

TABLE V

RESULTS IN SEMINOMA OF TESTIS

Years After Treatment	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Total No. of Patients	74	73	72	64	61	59	51	43	41	36	32	30	25	20	18	16	10	7	7	7
	75	75	75 96%	69	66 93%	65	57 90%	50	47	42 86%	38	36 83%	31	26	24 75%	22	15	12	12	12 59%
Extended Nodal Irradiation	53	51	51	50	46	46	39	32	29	25	23	21	16	12	10	9	3	0	0	0
	53	53	53 96%	52	49 96%	49	42 93%	35	32	28 89%	26	24 88%	19	15	13 77%	12	6 50%	2	2	2
Lymphadenectomy and Abdominal Irradiation	9	9	8	8	8	8	8	8	8	8	6	6	6	5	5	4	4	4	4	4
	10	10	10	10	10	10	10	10	10	10	8	8	8	7	7	6	6	6	6	6
Abdominal Irradiation Only	11	11	11	6	6	5	4	4	4	3	3	3	3	3	3	3	3	3	3	3
	11	11	11	6	6	5	4	4	4	3	3	3	3	3	3	3	3	3	3	3
Abdominal Irradiation With or Without Lymphadenectomy	20	20	19	14	14	13	12	12	12	11	9	9	9	8	8	7	7	7	7	7
	21	21	21 91%	16	16 88%	15	14 86%	14	14	13 85%	11	11 82%	11	10	10	9	9	9	9	9 78%

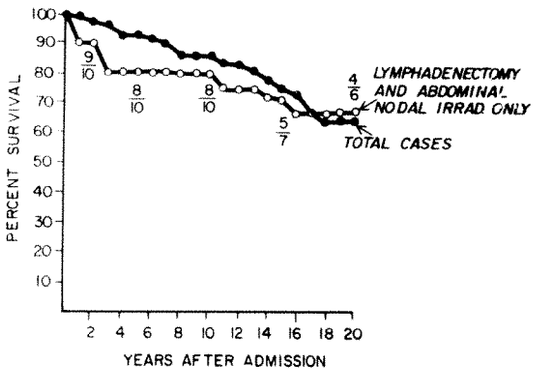


FIG. 11. Survival rates after lymphadenectomy and abdominal nodal irradiation only.

improve the disease-free survival of these patients with Stage I seminoma of the testis, compared to orchiectomy followed by irradiation alone. Although, our series is small as compared to that of Maier *et al.*, the results tend to agree with their conclusions. The retroperitoneal lymph node dissection in pure seminoma of the testis has no role in its management.

There are 11 patients who had irradiation to the ipsilateral inguinal and abdominal paraaortic lymphatics only, following simple orchiectomy (Fig. 10). All these patients survived without evidence of disease. At the end of 2, 3, 5, 10 and 15 years, there were 11, 6, 5, 3, 3, and 3 patients at risk, respectively. None of these patients have died either with or without the disease. The details of the results can be seen in Table v.

Of interest was a 36 year old white male, who was seen at Brooke General Hospital in January 1950 with a history of enlarged left testis. A left-sided orchiectomy revealed pure seminoma with no extension into the spermatic cord. Further investigations showed that he had left-sided hydronephrosis. He thus had Stage II disease on admission. He received radiation therapy to the left inguinal, and the abdominal paraaortic lymphatics up to the crura of the diaphragm. The total tumor dose was 2,400 rads in 12 treatments. He remained well for 2 years. He then showed evidence of metastatic disease in both lungs. He received further irradiation to the mediastinum, left supraclavicular fossa, and both lungs. The total midline dose in these areas varied from 1,500 rads to 1,800 rads at 220 kvp. and 15 ma. The patient was alive and well with no evidence of disease, when he was last examined in February 1972.

There are 53 patients who received radiation therapy to the ipsilateral inguinal, abdominal paraaortic, mediastinal, and left supraclavicular lymphatics following simple orchiectomy. At the end of 3, 5, 10, 15, and 17 years after their first admission the survival rates are 96, 96, 89, 77, and 50 per cent, respectively (Fig. 12).

Of interest was a 39 year old white male who was diagnosed to have had Stage I pure seminoma of the right testis in January 1965. He had simple orchiectomy followed by irradiation of the right inguinal, abdominal paraaortic, mediastinal, and left supraclavicular lymphatics in the usual manner. He remained well until July 1965 when he noticed swelling of his left testis. His chorionic gonadotropins in May 1965 were greater than 375 and less than 1,875 I.U./24 hr. Later tests showed even greater increase in chorionic gonadotropins. A simple orchiectomy on the left side revealed, as quoted from the Armed Forces Institute

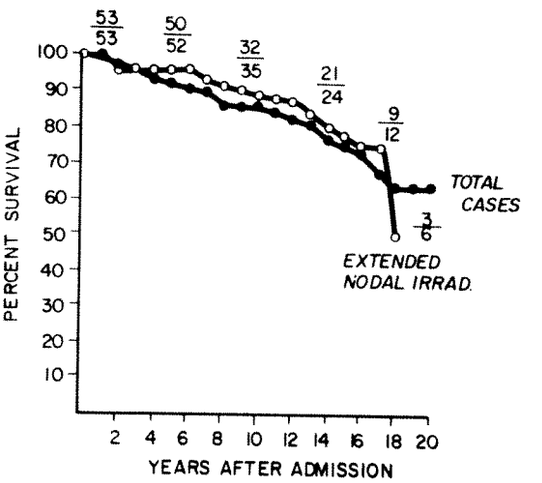


FIG. 12. Survival rates after extended nodal irradiation.

of Pathology (file number 1164480 of August 24, 1965), the presence of "embryonal carcinoma with foci of teratoma and syncytiotrophoblastic elements." At this time the slides on his right testis were also reviewed by the Armed Forces Institute of Pathology which reconfirmed the diagnosis of seminoma with anaplasia. The patient underwent retroperitoneal lymphadenectomy in August 1965, with none of the 44 lymph nodes being positive for metastatic disease. The patient is alive and well after 7 years, when he was last examined in February 1972.

The question naturally arises whether routinely irradiating the mediastinum and the left supraclavicular lymphatics in Stage I disease is justifiable, in order to either increase the survival or prevent future metastatic disease in these areas? Friedman,[3] Notter and Ranudd,[6] Castro and Gonzalez,[2] and Blady *et al.*[1] do not think so, based on their studies. However, Maier *et al.*[4,5] make a strong point of "prophylactically" irradiating the mediastinum and left supraclavicular lymphatics in Stage I disease. Assuming that the lymphadenectomy does not play any role in increasing the survival of patients with Stage I seminoma of the testis, one is quite justified in combining, in this study, the patients, who had abdominal paraaortic lymph nodes only irradiated either with or without retroperitoneal lymphatics, and comparing the survival rates of these patients with the survival rates of the patients who had extended nodal irradiation up to the left supraclavicular fossa routinely. One thus notes that there are 21 patients who had irradiation to the abdominal paraaortic lymphatics only with or without retroperitoneal lymphadenectomy (Fig. 13). At the end of 3, 5, 10, 15, and 20 years the survival rates are 91, 88, 85, 80, and 78 per cent, respectively. Although the total number of patients is small, one can quite justifiably say that the results are at least no worse, if not better, with irradiation of the abdominal paraaortic lymphatics group than the extended nodal irradiation group in Stage I patients with seminoma of the testis.

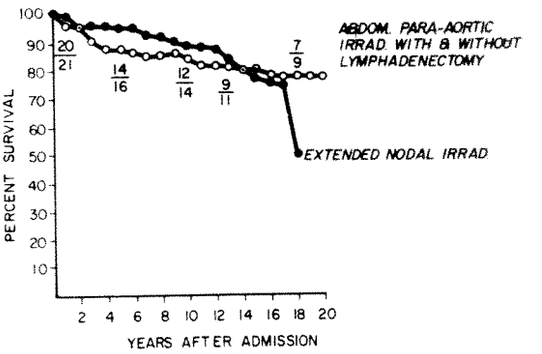


FIG. 13. Survival rates after abdominal paraaortic irradiation with and without lymphadenectomy.

SUMMARY

During the period of 1947 to 1969, 77 patients with pure seminoma of their testes were seen at Brooke General Hospital, Fort Sam Houston, Texas.

Most of the patients were younger than reported by other authors.

The right and left testis was involved with almost equal frequency.

All of our patients except 2 had a Stage I disease. Orchiectomy on the affected side was the method of biopsy routinely in all patients.

In this series no difference was noted in the survival rates of the patients who have had different kinds of treatments such as: retroperitoneal lymph node dissection and irradiation; irradiation to the abdominal paraaortic lymph nodes; and irradiation only of the abdominal paraaortic, mediastinal, and left supraclavicular regions.

The retroperitoneal lymph node dissection in pure seminoma of the testis has no role in its management.

There are also enough reasons to believe that routine irradiation of the mediastinum and the left supraclavicular region in a Stage I seminoma of the testis is not warranted.

It is suggested that a great effort should

be made to stage these patients with pure seminoma before any definite treatment is started. In a truly Stage I disease the cure rate should be close to 100 per cent, if managed adequately.

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SUPERVOLTAGE RADIATION THERAPY OF THE TESTICULAR TUMORS*

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FIVE years have elapsed since our previous review of results of treatment of the testicular tumors by the Stanford Division of Radiation Therapy.[4] The feasibility study of lymphadenectomy performed between 2 portions of a course of radiation therapy which had just begun at that time has continued, although the initial enthusiasm has somewhat cooled.[1,10] In addition, continued improvement in survival has been noted by the Royal Marsden group utilizing radiation therapy alone.[11] Thus, we felt a review of our feasibility study should be presented, although a firm decision on the value of this so-called "sandwich technique" will have to await the results of a randomized trial.

MATERIAL AND METHOD

All testicular tumor patients seen in Stanford University Radiation Therapy Division from the period 1956–1971 were reviewed. The former date corresponds with the installation of the Stanford Medical Linear Accelerator,[5,7] and with minor exceptions all patients were treated with 4.0, 4.8, or 6.0 mev. roentgen rays from that machine or Varian Clinacs. A relatively consistent, aggressive approach has been continuously in operation during that period, with 2 exceptions to be discussed later.

Staging has continued as previously described[4] with Stage I being assigned to patients whose only evidence of disease was in the testicle; Stage II, those with histologic evidence of disease at the resected end of the spermatic cord or evidence of retroperitoneal lymph node involvement; and Stage III, those with other abdominal organ involvement or spread beyond the abdomen. Until the accuracy of lymphangiography could be more adequately defined, surgical results have been used in staging. Pathology has not been systematically reviewed except that each has been confirmed by one of the Stanford pathologists. Since 1968 the British Testicular Tumor Panel classification[2] has been used. Prior to that time, that of Dixon and Moore[3] was in use. Because of this and the small patient groups resulting when 2 treatment techniques and 3 stages are used, the carcinoma patients are not further subdivided.

Table 1 presents the patient population. The relative proportion of seminomas to carcinomas is more nearly like the Canadian experience[8] rather than that seen in England.[2] The carcinoma patients are further subdivided into 2 treatment groups. The first are those treated until late 1965 when our feasibility study of the "sandwich technique" began. Prior to that time, all

TABLE I

DISTRIBUTION OF 214 TESTICULAR TUMOR PATIENTS AT STANFORD RADIATION THERAPY DIVISION 1956–1971

	No.	Per Cent
Seminoma	102	47.7
Carcinoma	80	37.4
Standard treatment	(48)	(22.4)
Sandwich treatment	(32)	(15.0)
Excluded	26	12.1
Other histology	6	2.8

* Presented at the Fifty-fourth Annual Meeting of the American Radium Society, in Joint Session with the James Ewing Society, and the Society of Head and Neck Surgeons, Boca Raton, Florida, May 14–19, 1972.
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TABLE II

EXCLUSIONS*

	Seminoma			Carcinoma	
	NED	*DOD*	*?*	*NED*	*DOD*
Treated elsewhere with follow-up at Stanford University Hospital only†	22, 16, 10			17	
Treated elsewhere with aggressive therapy for recurrence or extension‡	8, 9, 2	27		9	0
Treated elsewhere with retreatment for palliation only					0, 0, 0, 0, 0
Treated elsewhere; no treatment recommended					0, 0, 0, 0, 0
Consultation only	2, 0		0	4, 0	0, 0

* Time of survival in whole number of years; less than 1 year listed as 0.

† One patient with teratoma and seminoma of the left testicle (1948) and seminoma of the right testicle (1953) entered in both seminoma and carcinoma groups.

‡ Includes 1 carcinoma patient treated by 4 institutions over 5 months.

NED = no evidence of disease; DOD = dead of disease.

but 1 Stage II and one-half of the Stage I cases had had an attempted retroperitoneal lymph node dissection prior to referral. These are referred to as being treated with the standard technique. Since late 1965, the sandwich technique has been used.[4] Patients were excluded from this review because they were referred for follow-up only, for consultation only, or had had previous definitive treatment and subsequently recurred. Patients who had only an orchiectomy and were referred after distant disease became apparent were not excluded. Table II gives the details of these exclu-

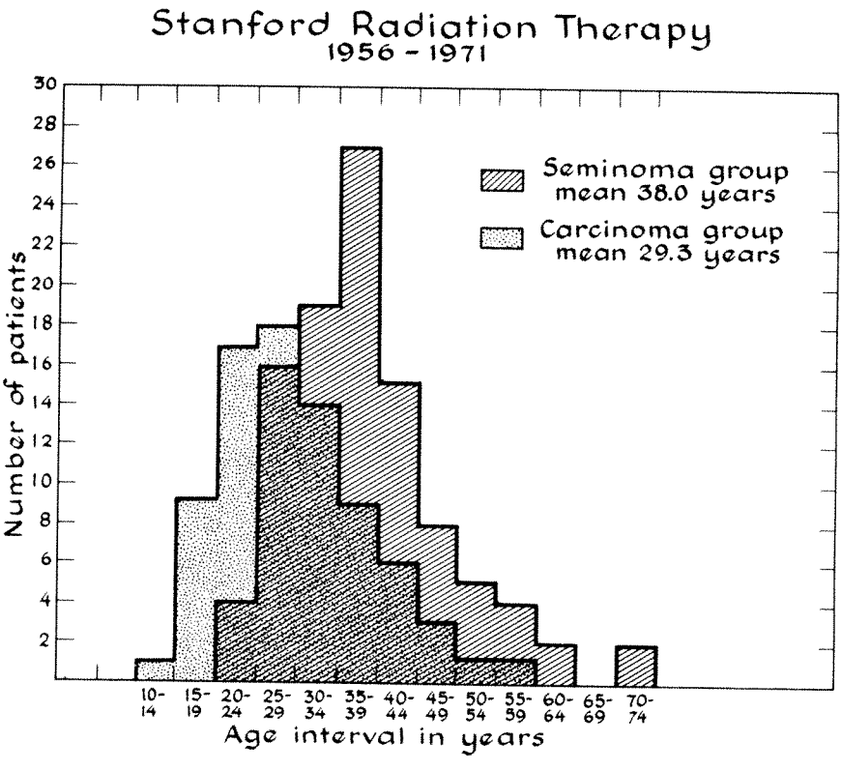


FIG. 1. Age distribution of 102 seminoma patients and 80 carcinoma patients.

sions. The tumors listed as other in Table 1 include an orchioblastoma, 2 interstitial cell tumors and 3 lymphomas.

Figure 1 presents the age distribution of the patients. The means are nearly 2 years older than in our previous report and now are nearly identical with the large Canadian series.[8] Confirming previous reports, 59.8 per cent of the seminoma patients had right testicular tumors (significantly different from 50.0 per cent at the 0.05 level), while 50.0 per cent of carcinomas occurred on the right.

Initial evaluation has included lymphangiography since 1962. Detailed results will not be reviewed at this time since Maier and Schamber[9] have recently reported on this facet, and our data also revealed diagnostic accuracy of 80 per cent. Inferior vena cavography and retrograde renal vein study are performed, if indicated. Full lung tomography with a compensating filter over the mediastinal structures is also used, especially preoperatively in the sandwich technique.

In the seminoma Stage I and those of Stage II cases with only cord involvement, the paraaortic and ipsilateral iliac lymph nodes are treated *en bloc* up to the diaphragm and down to the inguinal ligament by anterior and posterior opposing ports using supervoltage equipment. The total dose is 3,500 rads given at 1,000 rads per week. No further treatment is given. For the Stage II cases with abdominal lymph node involvement, prophylactic treatment is given to the mediastinum and bilateral supraclavicular regions. The same dose and fractionation are used. Stage III cases are treated aggressively and such treatment is individualized. With bulky paraaortic, mediastinal or supraclavicular lymphadenopathy or pulmonary metastases, whole lung irradiation is given to 1,500 rads in 3 to 4 weeks, while the lymph node-bearing areas above the diaphragm receive treatment similar to that of the abdominal lymph nodes. A 500 to 1,000 rads supplement may be given to bulky disease.

For Stage I and II carcinoma patients, 3,000 rads is given to the abdominal lymph nodes as is done for the seminoma patients. This is followed by a 3 week rest period at the end of which each patient is evaluated by an abdominal roentgenogram to study the dye-filled lymph nodes and full-lung tomography to search for pulmonary metastases. Usually within 2 weeks after bilateral retroperitoneal lymph node dissection, radiation therapy is resumed. Initially, the ports are the same as those used preoperatively; however, oblique fields are employed to deliver over 4,000 rads to the paraaortic lymph nodes. The total dose is usually 5,000 rads when the dissection is negative and 5,500 rads when positive. When the abdominal lymph nodes are involved, 4,500 to 5,000 rads is given to the mediastinum and supraclavicular regions. Stage III carcinoma patients have been managed on an individual basis, usually with similar treatment to lymph node areas, supplementary irradiation to large masses or pulmonary lesions, and frequently with prophylactic lung irradiation. More recently, in addition, we have referred these patients for adjunctive multiple drug chemotherapy.

In those cases where a scrotal exploration has been performed or tumor was present at the resected end of the spermatic cord, the iliac field is extended and bolus added or a separate orthovoltage field is added to include the hemiscrotum.

Data were processed with an IBM 360/50 computer, utilizing the Kaplan-Meier method.[6] Time was calculated from the initiation of radiation therapy. In addition to the usual actuarial survival curve, for reasons to be discussed later, curves were generated for the probability of disease-free survival. In each curve, unless indicated, a point represents 1 patient who either was at risk for the specified length of time or when the curve changes at a point, a patient has died or relapsed. Patients who never were felt to be free of disease are scored as relapsing at zero time. Patients with active disease or on chemotherapy were considered dead at their most recent

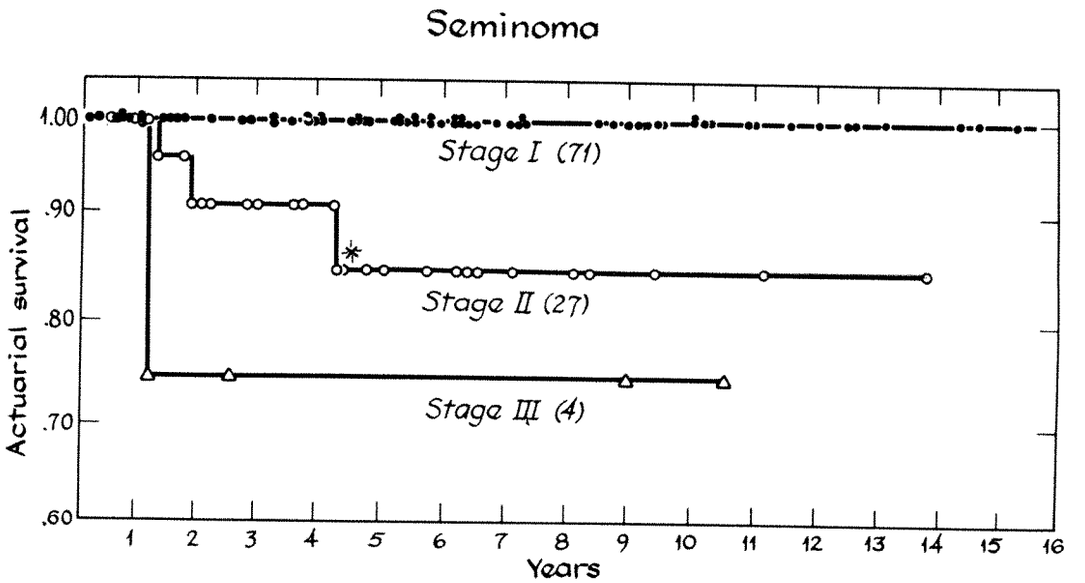


FIG. 2. Actuarial survival of 102 seminoma patients by stage (see Table III for numerical values). Numbers in parentheses refer to patients at risk. Each point refers to an event, either withdrawal or death. Asterisk refers to patient classed as not surviving, although alive without evidence of disease being maintained on chemotherapy.

follow-up. Patients who had received chemotherapy but have not been treated for at least 2 years and remain disease free, are scored as surviving or as being free of relapse for that period of time. Patients lost to follow-up or dying of intercurrent disease were withdrawn at that date. The survival figures are presented to 2 decimal points plus or minus the standard error where applicable.

RESULTS

Survival data are presented in Figures 2 through 7 and are summarized in Table III.

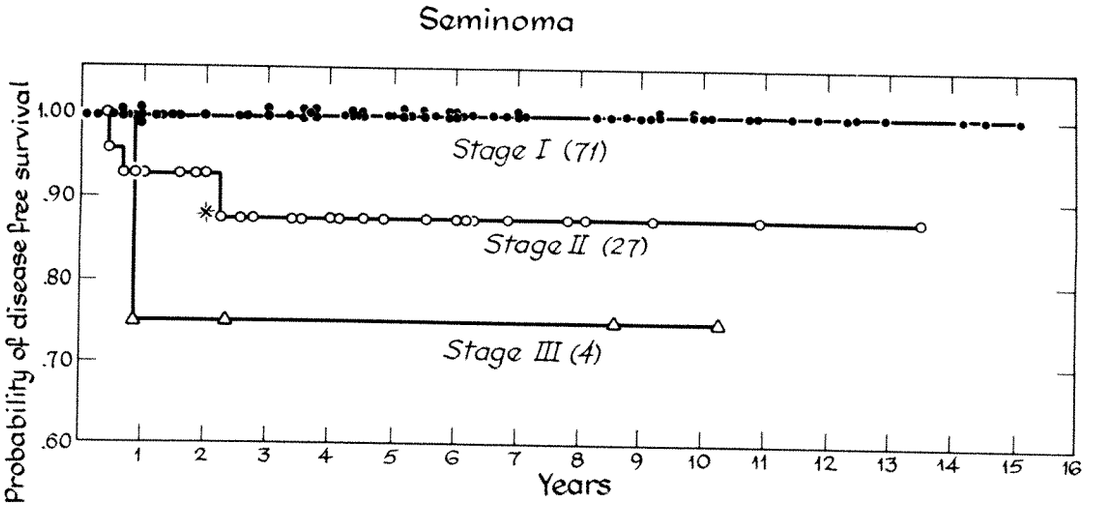


FIG. 3. Probability of disease-free survival of 102 seminoma patients (see Fig. 2). Asterisk refers to patient relapsing at 27 months being treated with chemotherapy.

Figure 2 depicts the survival for the seminoma patients. Survival for all 102 patients was .95±.01. Even in the presence of abdominal lymph node involvement, survival is 85 per cent (.85±.08). Frequently widely metastatic disease can be sterilized. Figure 3 emphasizes the usually early occurrence of relapse, but the occasional instance of delayed relapse. Figures 4 and 6 compare the survival of carcinoma patients treated by standard and sandwich techniques, respectively. The excellent results for Stage I cases treated by the sandwich technique has continued; however, approximately one-half of the Stage II cases succumb from their disease. One difficulty in comparing this technique with the standard treatment is that several of the latter Stage I cases did not have lymphangiography or retroperitoneal lymph node dissection. Since the criteria for identifying Stage III patients have not really changed, a comparison of the Stage I and II cases treated by each method might reveal a more valid comparison. Such survival for the 31 Stage I and II cases treated by the standard method is .67±.09 while the sandwich technique yields .57±.18 (Table III). Obviously, these results are not significantly different. It has become clear that a 2 year survival is no longer adequate for the evaluation of end results with the newer treatment techniques, as can be seen for the Stage II cases in Figure 6. It was for this reason that the disease-free survival was examined; Figures 5 and 7 present these data. Here it can be seen that 1 year of disease-free survival means that a patient has a *very* low risk for recurrence. The disease-free survival for the 2 treatment methods are .68±.08 for the standard, and .78±.07 for the sandwich technique. Again,

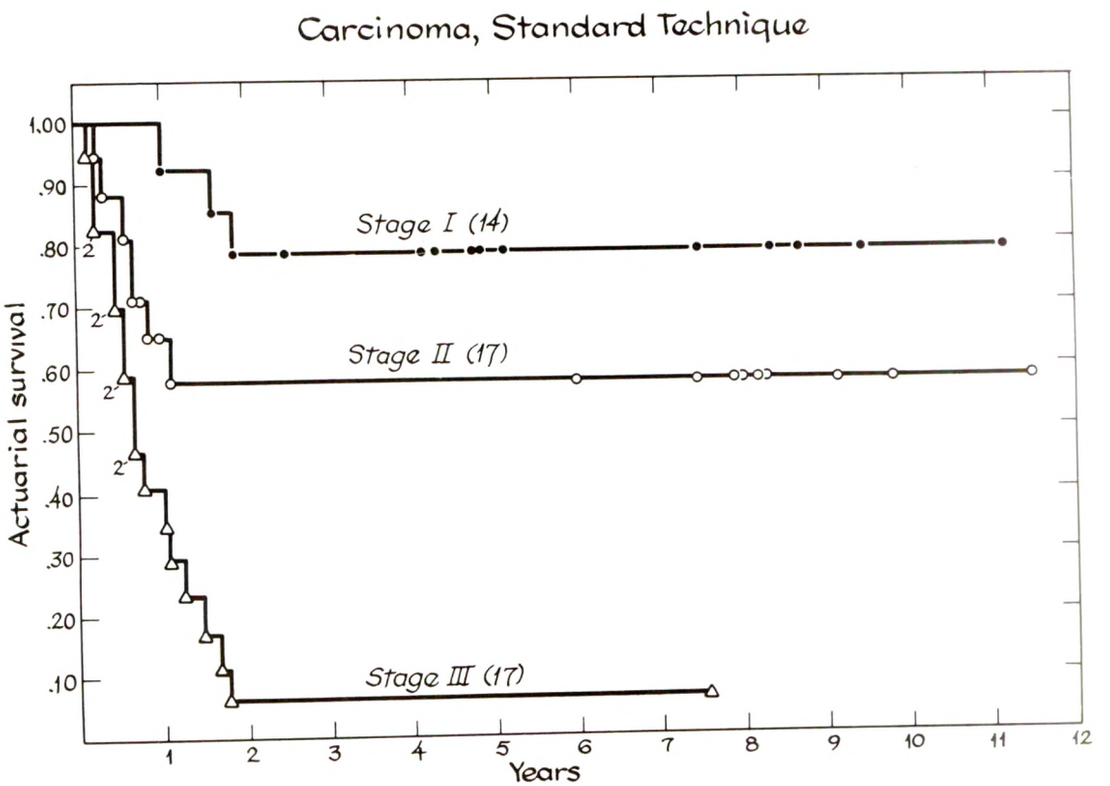


Fig. 4. Actuarial survival of 48 carcinoma patients treated with standard technique (see text). Numbers beside symbols refer to 2 events (deaths, in these cases) per point.

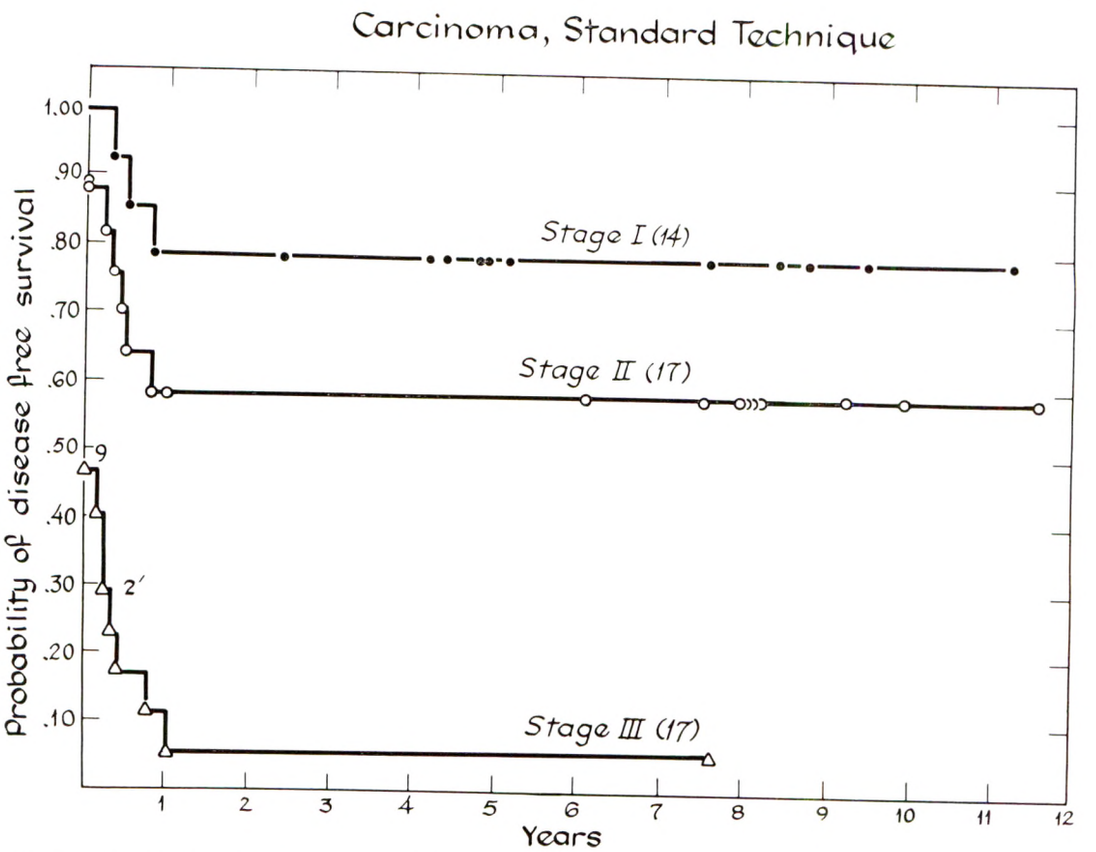


FIG. 5. Probability of disease-free survival for 48 carcinoma patients treated with standard technique.

these are not significantly different values.*

An additional point should be made with respect to the Stage I carcinoma group patients treated with the sandwich technique. Six of the 12 did not receive the full postoperative course. In 2, the total dose to the retroperitoneal lymph nodes was 3,000 rads and in the remainder 3,500–4,000 rads. In 4 cases the second portion of treatment was not given because of the negative lymph node dissection and the desire of the urologist or radiation therapist to discontinue it. In the 2 remaining cases this decision was made because the patient had

* The apparent difference between probability of disease-free survival and actuarial survival for the sandwich technique is due to the uncertainty of the figures. In the case of survival, the last event occurred when only 4 patients were at risk, whereas for probability of disease-free survival the last event occurred when 13 patients were at risk.

TABLE III

SUMMARY OF ALL CASES

	No. of Cases	Actuarial Survival	Probability of Disease-Free Survival
Seminoma, all cases	102	.95 ± .01	.96 ± .02
Stage I	71	1.00	1.00
Stage II	27	.85 ± .08	.88 ± .07
Stage III	4	.75 ± .22	.75 ± .22
Carcinoma, standard technique			
Stage I	14	.79 ± .11	.79 ± .11
Stage II	17	.58 ± .12	.59 ± .12
Stages I and II	31	.67 ± .09	.68 ± .08
Stage III	17	.06 ± .06	.06 ± .06
Carcinoma, sandwich technique			
Stage I	12	1.00	1.00
Stage II	20	.48 ± .17	.65 ± .11
Stages I and II	32	.57 ± .18	.78 ± .07

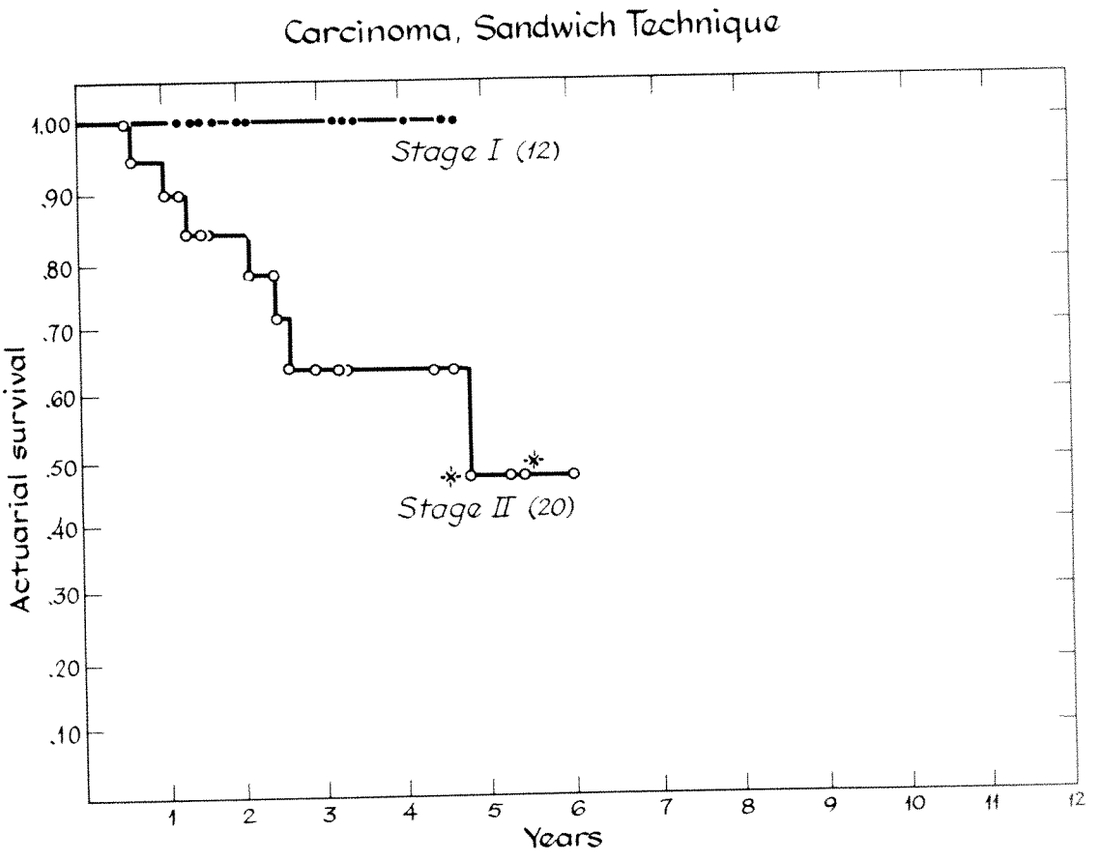


Fig. 6. Actuarial survival of 32 carcinoma patients treated with sandwich technique (see text). First asterisk represents a patient treated with chemotherapy for pulmonary metastases, alive, unmaintained for 18 months. The second asterisk represents a patient treated for pulmonary metastases, alive, unmaintained 5 years.

had persistent nausea and vomiting during the first portion of treatment.

Complications have been minimal in the seminoma patients and, in general, related to unusual treatment such as mild radiation pneumonitis when a large mediastinal mass was treated or subcutaneous fibrosis when it was believed that a Stage II carcinoma was treated. There were 2 instances of activation of duodenal ulcer, 1 of inflammatory band producing jejunal obstruction and requiring surgical intervention, and 1 patient with unexplained moderately severe right lower quadrant subcutaneous fibrosis. There was 1 unusual case, treated for Stage I seminoma, who developed severe retroperitoneal fibrosis causing ureteral obstruction and who had a demyelinizing disease as well as apparent gastrointestinal injury about 10 years after treatment. Finally, a patient treated elsewhere for a left testicular carcinoma necessitating high dose mediastinal irradiation was subsequently treated by us to the usual fields for a Stage I seminoma. Several years later he developed a fibrosarcoma in the mediastinal field.

The complications seen in the carcinoma group tend to be of higher incidence and somewhat greater severity. Those treated with standard technique have been described previously.[4] In the sandwich technique retrograde ejaculation is universal but we have also noted 2 instances of small

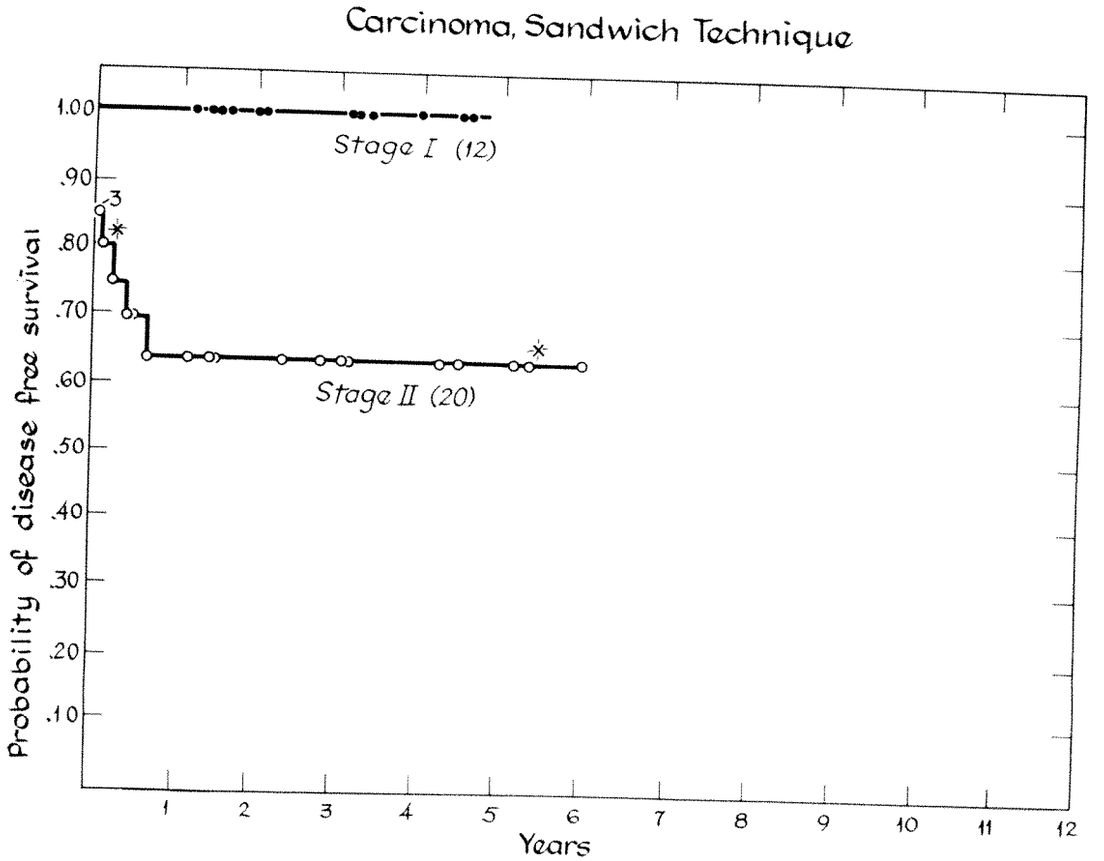


FIG. 7. Probability of disease-free survival of 32 carcinoma patients treated with sandwich technique (see Fig. 6).

bowel obstruction managed medically, 3 cases requiring lysis of adhesions, and 1 instance of delayed wound healing.

DISCUSSION

Supervoltage irradiation in the aggressive manner described appears to be curing a very large proportion of patients with seminoma, even when the disease is far advanced. We have not irradiated above the diaphragm in the absence of paraaortic lymph node involvement and have not had such a patient develop recurrence.

The value of the sandwich technique when compared to irradiation alone remains an open question. It does allow us to separate patients who do very well from those who will do less well (*i.e.*, have about a 35 per cent chance of recurrence or approximately 50 per cent likelihood of survival). Perhaps a prophylactic, multiple drug chemotherapy trial for these selected patients would improve their survival. The randomized trial, underway at Walter Reed Hospital, will hopefully provide significant answers to the value of the sandwich technique.

The question of whether there is a difference between irradiation alone and lymphadenectomy for the carcinomas has really not been discussed recently. Caldwell[1] considered the problem in 1969 and concluded that a careful cooperative trial of irradiation alone, irradiation as in the sandwich technique and lymphadenectomy with postoperative irradiation was long overdue. The Walter Reed randomized trial of irradiation alone compared with the sandwich technique will hopefully answer half of this question. Recent results

of lymphadenectomy alone appear to require that the second half be similarly approached.[12,13] However, both series are highly selected as can be seen by the fact that about two-thirds of each had negative retroperitoneal lymph nodes, while less than one-half of the Stage I and II cases in this series were Stage I. Further, in the review of Walsh *et al.*[13] over half the cases received radiation postoperatively. Certainly, with the excellent results obtained by Smithers *et al.*[11] one cannot conclude at this time that aggressive supervoltage irradiation alone in the carcinoma group of patients can be surpassed by any other method of treatment.

The value of analyzing data by means of the probability of disease-free survival curves should be stressed. When we compare the standard technique *versus* the sandwich technique in carcinoma patients (Fig. 4; and 6) using survival, it becomes apparent that the rate at which failure appears in the Stage II cases is considerably less rapid for the sandwich technique. With that technique 2 year survival results are totally inadequate for evaluating end results. On the other hand, for probability of disease-free survival (Fig. 5; and 7) 1 year would seem sufficient for this small group of patients. For survival, the last event occurs at more than 2 years, while for probability of disease-free survival, the last event occurs at 8 months.

SUMMARY

An aggressive approach to the treatment of testicular seminomas, utilizing supervoltage techniques, has resulted in 95 per cent survival for all stages.

For the carcinoma group the sandwich technique has resulted in a sharper segregation of the Stage I and II cases with respect to survival with 100 per cent survival resulting in Stage I.

Adjunctive chemotherapy may well be warranted in Stage II, where about one-third to one-half of the patients develop relapse or die.

The value of analyzing such data by means of probability of disease-free survival is emphasized.

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PRE-ESTROGEN IRRADIATION OF THE BREAST TO PREVENT GYNECOMASTIA*

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ESTROGEN therapy is widely used in treatment of prostatic cancer. The side effect of gynecomastia along with nipple and breast hypersensitivity and their accompanying psychologic effect has caused additional discomfort and anxiety in these patients. The prophylactic use of irradiation to the breast prior to estrogen administration has helped to significantly decrease these side effects.

Larsson and Sundbom[5] were the first to apply the effects of radiation in male breasts to prevent enlargement of breast tissue subsequent to estrogen administration. Since that time several other papers including one by the authors have been reported.[1–4,6]

A previous paper published by this institution in 1969 reported 20 patients; 50 additional patients are now presented bringing the total to 70. Questionnaires were sent out and charts were reviewed for the additional 50 patients. There was a 90 per cent response to the questionnaire. Questions were related to: (1) side effects immediately consequent to the radiation treatment itself such as skin discomfort and pain; (2) development of gynecomastia; (3) increased sensitivity and tenderness in the nipple and breast after radiation treatment and subsequent estrogen administration.

The age of the patients ranged from 49 to 82 years and all had a histologic diagnosis of carcinoma of the prostate. Follow-up ranged from 1 to 36 months with the average being approximately 11.2 months.

Table I illustrates the data of the new group. Table II gives a compilation of the total number of patients including those previously reported.

A surface dose of 900 r was given to each breast in a single fraction. Two techniques were employed: (1) 100 kv., half value layer 2.4 mm. Al, focal skin distance of 22 cm., and a cone diameter of 5 cm.; and (2) 280 kv., half value layer 0.5 mm. Cu, focal skin distance of 50 cm., and a cone diameter of 5 cm.

DISCUSSION

Our experience has been similar to that of Alfthan and Kettunen[2] in having poor results with patients already taking estrogen prior to irradiation. Therefore, patients diagnosed initially at our institution are given the radiation therapy prior to estrogen administration.

Only 1 patient had such severe gynecomastia and breast pain that estrogen therapy was discontinued. The remainder were not unduly affected by the breast pain, tenderness and gynecomastia, and in fact

TABLE I

DATA OF THE NEW GROUP OF 50 PATIENTS

	None	Minimum	Moderate	Severe
Skin changes and pain related to irradiation	49	1	0	0
Gynecomastia	33	5	11	1
Breast and/or nipple pain and/or tenderness	27	4	18	1

* From the Departments of Radiation Therapy and Nuclear Medicine, The Cleveland Clinic Center, Cleveland, Ohio.

TABLE II

DATA OF THE TOTAL NUMBER OF 70 PATIENTS

	None	Minimum	Moderate	Severe
Skin changes and pain related to irradiation	64	3	2	1
Gynecomastia	51	8	11	1
Breast and/or nipple pain and/or tenderness	44	7	18	1

only 2 volunteered such complaints without being directly questioned.

CONCLUSION

Irradiation of the breasts is a safe and effective means of controlling the undesirable side effects of estrogen therapy for prostate cancer.

Seventy patients have now been treated at this institution and the beneficial results derived are listed in the tables.

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HEMORRHAGIC CYSTITIS AND VESICOURETERAL REFLUX SECONDARY TO CYTOTOXIC THERAPY FOR CHILDHOOD MALIGNANCIES*

By WILLIAM A. RENERT, M.D., WALTER E. BERDON, M.D., *and* DAVID H. BAKER, M.D.
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STERILE hemorrhagic cystitis can occur following the use of cytotoxic drugs, most notably cyclophosphamide.*[4,10,11,13] The cystitis may be either an acute inflammation or a chronic, relapsing hemorrhagic form which persists even after removal of the drug.[3,7] Vesicoureteral reflux is a common coexistent finding. The roentgenologic picture of nodular defects in the bladder must not be confused with involvement of the bladder by the primary disease.

Three cases of hemorrhagic cystitis in children are reported, 2 of which resulted from cyclophosphamide and the third from cytosine arabinoside,† not previously reported to cause cystitis. Vesicoureteral reflux was noted in 2 of the patients.

REPORT OF CASES

CASE I. D.P., a 4 year old girl, presented with an abdominal mass. Exploratory laparotomy revealed a ganglioneuroblastoma, which was partially resected and then treated with radiation therapy. Four years later her urinary catecholamines were elevated, but exploratory laparotomy failed to disclose any tumor. A year later a lytic lesion was discovered in the spine, with a block on myelography, and she was treated with laminectomy and radiation therapy. A bone marrow examination revealed 85 per cent tumor cells, and chemotherapy with vincristine, cyclophosphamide and steroids was begun. Cyclophosphamide was given intravenously at 10 mg./kg. for 5 days with vincristine at 0.05 mg./kg. given at weekly intervals. This had been given almost continuously for 14 months when hematuria began, initially mild and intermittent, but then becoming more severe, requiring many transfusions. Urine cultures were negative.

Cystoscopy showed subacute cystitis subepithelial telangiectasia and ecchym An intravenous pyelogram revealed no upper urinary tracts, but the bladder was tracted with edematous mucosa. A cystog showed bilateral vesicoureteral reflux, and post voiding study again showed "thu printing" defects in the bladder wall (Fig The roentgenogram of the distended bla did not show the bladder defects as well a post voiding study (Fig. 2). The cyclop phamide and vincristine were discontinued the severe hematuria has continued ov 2 year period, requiring multiple transfu with frequent fulgurations of the bladder.

Comment. The hemorrhagic cystiti this case is an example of the chronic f with telangiectasia causing recurrent h orrhage despite discontinuance of the d The vesicoureteral reflux probably re from elevation and deformity of the tri of the bladder.

CASE II. C.P. was a normal male born

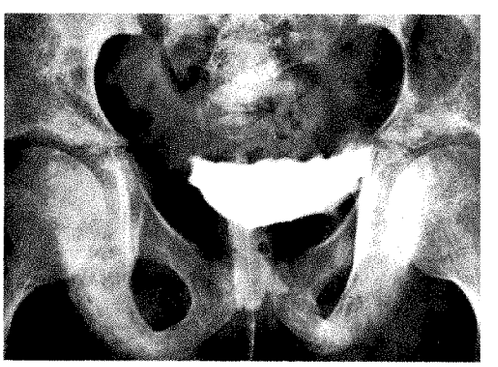


FIG. 1. Case 1. D.P. (188 16 38.) A 10 year ol with disseminated osseous metastases from n blastoma. Post voiding study, during a cy raphy, shows irregular nodular defects ("th printing") in bladder wall.

* Cytoxan® Mead Johnson.
† Cytosar® Upjohn.

* From the Department of Radiology, Columbia-Presbyterian Medical Center Babies Hospital, New York, New York.

mother who had had bilateral retinoblastomas removed as an infant. At 1 year of age he was noted to have bilateral retinoblastomas. A bone marrow examination was negative, and he received 3,500 rads to both eyes over 20 days. Following several recurrences treated with photocoagulation, the right eye was removed at age 2 years. A year later hepatosplenomegaly was noted, and a bone marrow examination revealed infiltration with tumor cells. He was treated at weekly intervals with injections of cyclophosphamide at 10 mg./kg., alternating weekly with vincristine 0.05 mg./kg. He lost vision in his left eye and received 3,500 rads again to both orbits. Multiple osseous metastases developed in spite of chemotherapy, and his cyclophosphamide was increased to 175 mg. a day orally, for 2 weeks. Over the next few months he received similar courses of cyclophosphamide, lasting 2 weeks to a month. Three weeks after the cyclophosphamide was increased, hematuria was noted. In the 10 days prior to admission, the hematuria became gross with the passage of numerous clots. Severe dysuria and colic developed with subsequent anuria. An intravenous pyelogram showed bilateral obstructive hydronephrosis. The bladder was deformed, although not well seen. A cystogram, at the time of the intravenous pyelogram, revealed a contracted bladder with deformity and intramural defects, and marked ureterovesical reflux with elevation of the trigone. In addition, there were clots in the bladder (Fig. 3). Cystoscopy showed bullous edema of the bladder mucosa. The cyclophosphamide was discontinued, and the hematuria cleared. A repeat intravenous pyelogram 1 week later showed good visualization and less dilatation of the upper tracts. The bladder was pear-shaped, but the mural contour defects were no longer present (Fig. 4). He was put on triple therapy with actinomycin D, chlorambucil, and methotrexate, but developed diffuse gastrointestinal hemorrhage and died. No autopsy was performed.

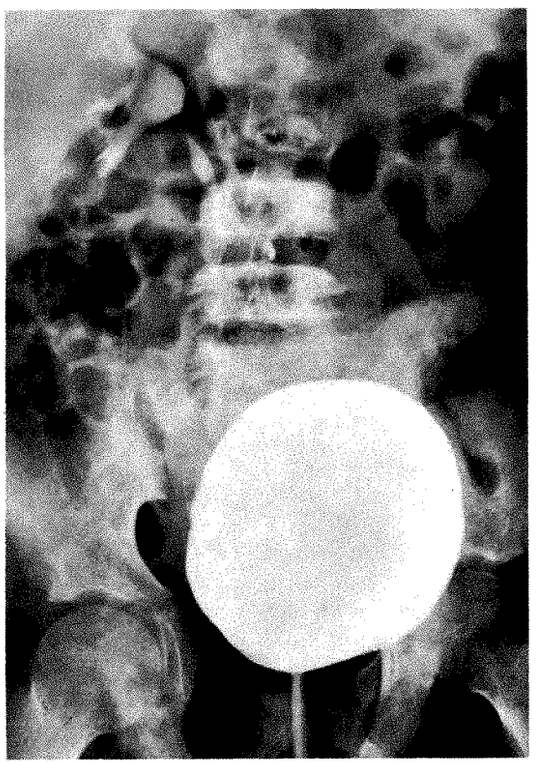


Fig. 2. Case 1. The same study as in Figure 1, with the bladder distended. Ureterovesical reflux on the right is seen, but the mucosal abnormality is obscured. Diagnosis—cystitis secondary to cyclophosphamide.

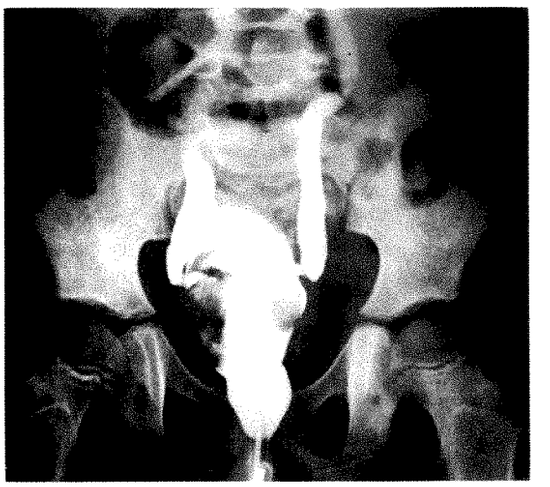


Fig. 3. Case 11. C.P. (183 06 13.) A 3 year old boy with metastatic retinoblastoma. Intravenous pyelogram had shown bilateral hydronephrosis and decreased concentration. The cystogram shows bilateral ureterovesical reflux, a contracted bladder with large contour defects, and elevation of the trigone.

Comment. This may represent a case of hemorrhagic cystitis which was dose-related, as it did not develop until the cyclophosphamide was markedly increased. It could not be determined whether the changes in the bladder would have pro-

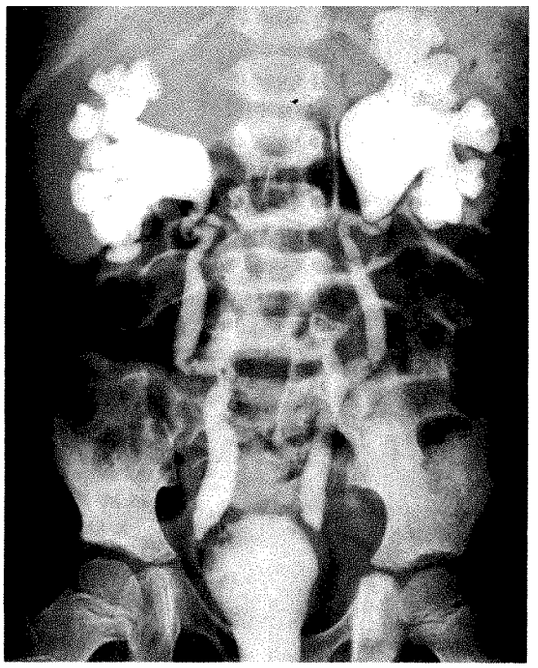


FIG. 4. Case II. One week later, the intravenous pyelogram shows good visualization of less dilated upper urinary tracts. The bladder has a restrictive outline, but the mural defects have disappeared. Diagnosis—cystitis secondary to cyclophosphamide.

gressed to fibrosis, as the patient died before a follow-up cystography could be performed. No autopsy was obtained.

CASE III. E.M. was well until age 2 when she developed bronchopneumonia. Physical examination at that time revealed hepatosplenomegaly but no significant lymphadenopathy was felt. The hematocrit was 33 per cent and the white blood cell count (WBC) was 95,000. The platelet count was 9,000 and a bone marrow examination was interpreted as subacute granulocytic leukemia. She was begun on cytosine arabinoside along with penicillin and sulfisoxazole for pulmonary infiltrates. She received 22 mg. of cytosine intravenously each day for 5 days and then 44 mg. for 5 days. Her WBC decreased to 9,000. A urinalysis at this time was normal. She received intermittent cytosine arabinoside over the next 2 months, 66 mg. intravenously every 2 weeks. Occasional vomiting was noted, but no other side effect from the cytosine. However, 3 months after cytosine arabinoside was begun, gross hematuria was noted. Urine culture was negative. An intravenous pyelogram revealed mild left ureteral dilatation, and the bladder had external pressure effect and nodular defects in its left wall (Fig. 5). Cystoscopy showed submucosal hemorrhage and edematous mucosa. The cytosine arabinoside was discontinued, and the hematuria stopped: 6 mercaptopurine was begun, but she was admitted 2 months later with massive gastrointestinal hemorrhage and intermittent seizures. She expired shortly after admission.

Autopsy showed a thickened bladder wall with focal, subepithelial hemorrhage, but no evidence of fibrosis or other chronic changes.

Comment. Sterile hemorrhagic cystitis has not been previously reported following cytosine arabinoside. This was the only medication the patient was on when the hematuria developed. The changes were acute, as no evidence of fibrosis was seen at autopsy, performed 2 months after the cytosine was discontinued.

DISCUSSION

Cyclophosphamide was developed in 1957[1] and shortly thereafter the association with sterile hemorrhagic cystitis was reported.[4,10,11,13] The etiology of the cystitis is not completely understood. Cyclophosphamide is converted in the liver by a convert-

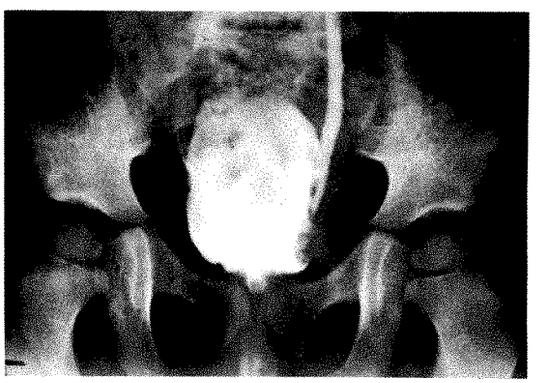


FIG. 5. Case III. E.M. (182 89 45.) A 3 year old girl with subacute granulocytic leukemia. A close-up of the bladder at the time of intravenous pyelogram shows external pressure effect and mural defects on left wall with mild left ureteral dilatation. Diagnosis—cystitis secondary to cytosine arabinoside.

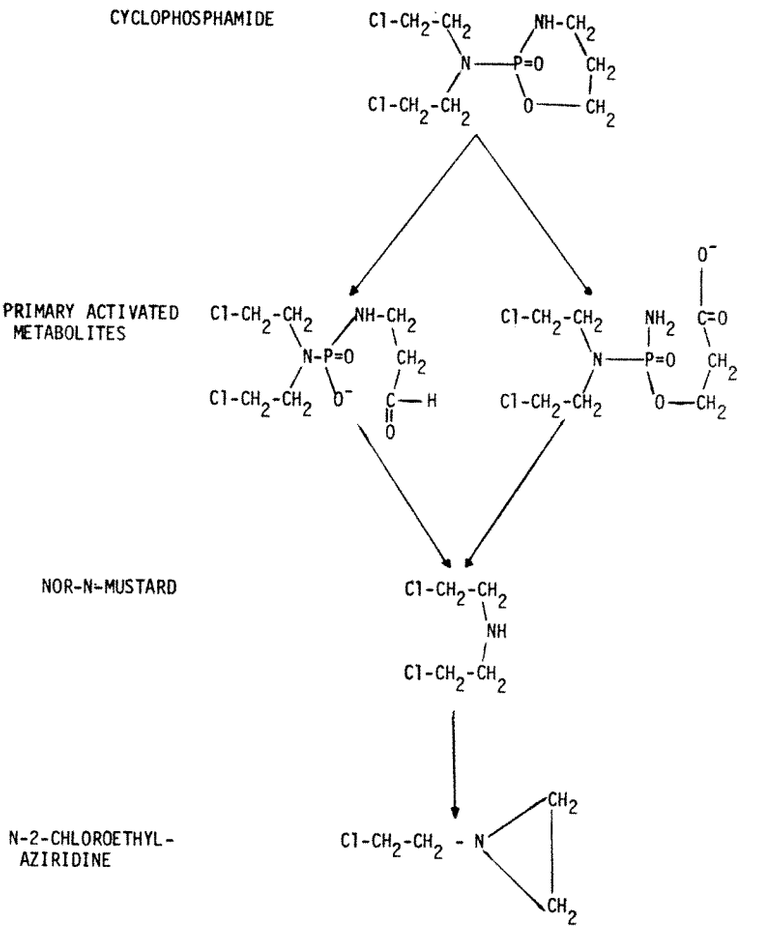


Fig. 6. Metabolic pathway of cyclophosphamide.

ing enzyme, phosphamidase, into primary active metabolites (Fig. 6), which exert the cytoxic effect and alkylating action. The activated metabolites are then converted to Nor-N-mustard and N-2-cholorethyl-aziridine[2] and excreted in these forms. It is probably one of these primary or secondary metabolites that causes the hemorrhagic cystitis. It is likely a direct action of the drug in the urine on the mucosa of the bladder, since urine taken from a dog receiving intravenous cyclophosphamide, and induced in a retrograde manner into another dog, can produce cystitis in the second dog.[12]

The type of hemorrhagic cystitis induced by cyclophosphamide has been classified into an acute and chronic form. The chronic form, which usually does not occur before 3 months of therapy with cyclophosphamide, may result in a fibrotic, contracted bladder. It is directly related to dose and length of administration. The fibrosis begins in the lamina propria of the bladder and spreads into the innermost smooth muscle fascicles, separating and replacing them. This results in reduced elasticity, and the bladder is unable to contract normally.[7] Telangiectasia is present (Fig. 7). These patients continue to bleed in spite of discontinuing the drug. Case 1 reported here is an example of this form.

The acute type can occur at any time of therapy, but most commonly occurs within

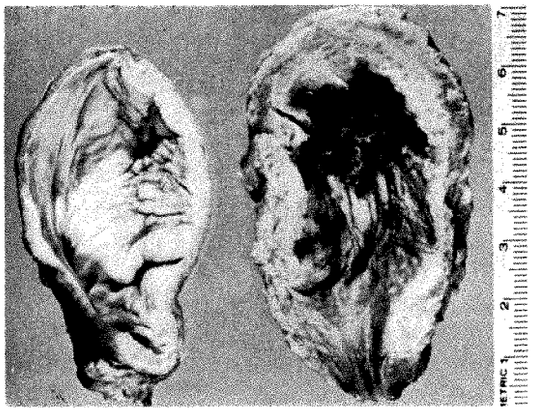


FIG. 7. A fibrotic, contracted urinary bladder is shown from a patient receiving a high dosage cyclophosphamide. A normal control bladder from a patient of the same age is shown on the left. (Courtesy of Warren W. Johnson, M.D., Memphis; and reprinted with permission from the *New England Journal of Medicine*.)

48 hours after a massive intravenous infusion of cyclophosphamide. The high amount of the active metabolite found in the bladder after intravenous infusion compared with the slowly increasing excretion with oral administration may account for the earlier symptoms occurring with the intravenous route.[5] The acute changes last from 4 to 5 days and clear after removal of the drug.[3,7]

The mechanism of action of cytosine arabinoside causing the hemorrhagic cystitis in Case III, reported here, is not known. Only a small portion of the cytosine appears in the urine, the major excretion product being uracil arabinoside.[14] Bladder changes were not reported in the original toxicity studies on cytosine arabinoside. The major side effects have been hematopoietic toxicity as well as nausea and vomiting. Mucosal ulceration and central nervous system effects were rarely observed.[6,8,9,15]

The roentgenologic picture of hemorrhagic cystitis varies with the severity of the changes in the bladder. Nodular defects seen on cystogram reflect hemorrhage and edema, and they must not be confused with involvement of the bladder by the primary disease. In some cases cystoscopy may have to be performed to exclude involvement of the bladder by the malignancy. Marked contracture of the bladder, elevation of the intertrigonal ridge and obstruction of the ureters is seen in chronic cases, and vesicoureteral reflux, seen in Cases I and II in this report, has also been described.[4,10]

SUMMARY

Three cases of sterile hemorrhagic cystitis following cytotoxic drugs used for childhood malignancy are described; in 2 cases associated with cyclophosphamide, vesicoureteral reflux was noted

One of the cases resulted from cytosine arabinoside, not previously reported to cause hemorrhagic cystitis

The roentgenologic findings are described, and emphasis is placed on differentiation from involvement of the bladder by the primary malignancy.

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WHOLE BODY AND PARTIAL BODY RADIOTHERAPY OF ADVANCED CANCER*

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CINCINNATI, OHIO; DETROIT, MICHIGAN; AND MEMPHIS, TENNESSEE

THE purpose of these investigations has been to improve the treatment and general clinical management and if possible the length of survival of patients with advanced cancer. Systemic effects of radiation therapy have been given particular attention in our work.

In the period February 19, 1960, through August 31, 1971, 85 adults were given whole or partial body radiation as therapy for far advanced cancer.

This paper will report on the survival of patients in 3 categories: colon; lung; and breast.

Prophylactic whole body radiation therapy was given to 3 children with localized Ewing's sarcoma and this experience will be discussed briefly.

Investigations of biochemical, cytologic and psychologic tests have been reported elsewhere.[8,11,50]

Our experience with the adjuvant use of autologous bone marrow will also be described.

ANIMAL STUDIES

The animal investigations basic to our work stem from the studies of Hollcroft *et al.*[13–15] These authors demonstrated better tumor regression when whole body irradiation was preceded by localized radiation therapy than when localized radiation therapy was given alone both for lymphoma and carcinoma in mice. The studies of Jacobson *et al.*[18,19] showed the importance of shielding of the spleen and other organs and parts of the body in preventing high dose radiation lethality in the mouse.

BRIEF REVIEW OF TOTAL BODY IRRADIATION IN MAN

Total body irradiation was first employed in 1923 by Chaoul and Lange.[7] Its use in 270 cases over the next 20 years was reviewed by Medinger and Craver.[32] These authors found the greatest palliation in the lymphomas and myeloproliferative diseases, but also noted improvement in multiple myeloma. Thirty-five patients with advanced carcinoma or sarcoma were included in this series, most of them receiving their total body radiation between 1931 and 1933.

Loeffler *et al.*[30] compared total body irradiation in single doses up to 150 r with nitrogen mustard and triethylene melamine and found that neither chemotherapy nor radiotherapy differed in hematologic effects, but that the patients receiving radiation did not experience the malaise of varying severity noted by all patients receiving the chemotherapeutic agents. Subjective improvement was noted only in the radiotherapy group.

Collins and Loeffler[9] gave total body irradiation in single exposure up to 200 roentgens and found this form of systemic therapy "a useful addition to the management of advanced cancer." The malignancies treated included lymphoma, chronic

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myelogenous leukemia and multiple myeloma.

Interest in total body irradiation in the treatment of Ewing's sarcoma, a tumor of children which carries a high mortality, has been aroused by reports from Milburn *et al.*,[33] Jenkins *et al.*,[21] and Rider and Hasselback.[39] In a small series so treated, survival appeared to be moderately improved compared to larger series treated by conventional local radiotherapy and/or ablative surgery. These groups felt further evaluation of this form of therapy to be most important.

Additional data have been published by the Medical Division of Oak Ridge Associated Universities,[1] concerning total body radiation therapy of lymphoproliferative and myeloproliferative disease.

Summaries of the frequent use of total body irradiation for the therapy of leukemia appear in an article by Buckner *et al.*[4] and in a comprehensive review of bone marrow transplantation by Bortin.[3]

Whole body radiation in routine clinical therapy has been and is currently used for leukemia,[23,53] lymphoma,[22–26,53] Hodgkin's disease,[3] polycythemia vera,[5] cancer of breast,[31] cancer of thyroid,[5] cancer of prostate,[10,31] and multiple myeloma.[9,32] Such therapy may be given by external radiation therapy (as in this particular study) or in the form of various radionuclides.

STUDY DESIGN

The studies reported here were initially considered as being in Phase I (to determine whether the treatment was toxic or not) and subsequently as Phase II (whether treatment appears effective or not but without controls). In reviewing these data it has been possible to find some comparable material in the literature. In one category, cancer of bronchus, comparable data were available in our institution.

INFORMED CONSENT AND INSTITUTIONAL REVIEW

All patients gave informed consent in accordance with directives of the Faculty Research Committee of the University of Cincinnati College of Medicine and those of the National Institutes of Health. The use of formal informed consent forms in this study antedated the above requirements by 2 years. The project is reviewed and approved regularly by the above Committee.

ELIGIBILITY OF PATIENTS

Patients become eligible for this form of treatment if they have advanced cancer for which cure could not be anticipated. Three children with localized Ewing's tumor at Children's Hospital were given whole body radiation as part of the curative attempt after the primary tumor had been ablated with local radiotherapy.

Biopsy proof of the malignancy has been established in all instances. Clinical data in each case have been reviewed by several physicians to be certain that the tumor had indeed extended from its primary site and that curative therapy was not applicable. This preliminary evaluation is followed by an observation period of 7–14 days to observe the general condition of the patient and to carry out baseline laboratory tests to be as certain as possible that the condition of the patient is relatively stable. Frequently this determination is difficult since the patients have serious illnesses of long standing and often have had considerable previous therapy.

Patients remain in the hospital as long as is necessary. Prior to the use of autologous bone marrow transfusion, hospitalization was occasionally as long as 8–10 weeks. Length of stay was also dependent upon the severity of the clinical manifestations stemming from the cancer. With the use of partial body irradiation and bone marrow infusion, hospitalization has been greatly shortened. The follow-up procedure is continuous during the lifetime of the patient.

A total of 112 subjects were initially entered in the study through August 31, 1971. During the screening period of 7–14 days, 24 of them (21 per cent) were not continued in the study and did not receive whole or partial body irradiation. Chief

among the reasons for elimination was an indication in the pretreatment phase that some risk from wide-field radiation might ensue or that another method of treatment was considered preferable. In some, a very rapid progress of the disease made inclusion undesirable. The treatment was completed in 85 adults and 3 children between April 1960 and August 31, 1971. Three patients have received 2 separate courses of treatment in this program. Follow-up time for survivors is reported through August 31, 1972.

PATIENT DOSIMETRY

The radiation is delivered by a cobalt 60 teletherapy unit under the following exposure conditions: The beam is directed horizontally at a wall 342 cm. away with the midline of the patient at 286 cm. from the source. For whole body exposures, the radiation beam size for the 60 per cent isodose curve at the patient midline distance is a square approximately 120 cm.×120 cm. The patient is placed in the sitting position with legs raised and head tilted slightly forward. Radiation is given by delivering half the specified exposure laterally through one side of the patient, the patient is then turned and the other half exposure delivered laterally through the other side. The combined dose of the 2 radiation fields provides a good homogeneous dose distribution through the patient. The maximum variation in lateral dose distribution was ±13 per cent for 1 patient who had a lateral trunk dimension of 36 cm.

The exposure to the patient is determined using a percentage depth dose table corrected for the source-to-skin distance used for the patient. Using the corrected depth dose at patient midline (1/2 lateral dimension at the trunk in the plane of the xiphoid) and a conversion factor of 0.957 rads/roentgen for cobalt 60 gamma radiation, the midline air exposure required to give a desired midline absorbed dose in rads is calculated. The validity of this procedure was established with measurements in an Alderson Rando Phantom using thermoluminescence dosimeters. Over the course of the study, the air exposure rates at the distance indicated above varied from 3 to 6 per minute.

For individuals receiving partial body radiation, the teletherapy collimator is used to restrict the beam. The xiphoid is used as the boundary of the field for upper and lower body exposures. The lateral dimensions of the patient in the plane of the xiphoid is again used for calculating the desired midline dose. As for the whole body exposure, the dose is delivered bilaterally. Additional information on the dosimetry aspects of this study has been published by Kereiakes *et al.*[27]

ANALYSIS OF SURVIVAL DATA

In considering the survival data there was a lack of consistent selection bias both in recommendation that a patient be eligible for treatment and in regard to the dose. The principal investigator had no part in determination of therapy in any given case except for outlining the general principles of the therapeutic regime. The choice in the case of each patient was made by several radiation therapists, 3 having been associated with the project during the 10 year period. In addition, 2 internists have had active roles in the selection and medical care of each patient. The dose of radiation to be given was decided upon by the radiation therapist in consultation with the internist.

There are 3 categories of patients (those with carcinoma of the colon, lung and breast) which are large enough to permit some analyses of survival. Each group will be discussed separately.

Survival data are given in days from the diagnosis of far advanced disease, since this convention has been used frequently in the literature and permits comparison of our survival data with published reports.

CANCER OF THE COLON AND RECTUM

Twenty-nine patients with this tumor comprised the largest single category (Table 1). In all cases the patients were classed

TABLE I

CANCER OF COLON—ALL CASES BY LENGTH OF SURVIVAL OF ADVANCED DISEASE

(29 Patients)

Study No.*	Age	Sex/Race	Survival After D_x (days)	Survival After R_x (days)	Dose† (rads)
106	58	F /W	40	25	300 LB
109	56	M/W	116	80	300 LB
052	60	M/W	120	91	200 LB
033	64	M/N	126	86	100
082	49	F /N	136	33	300 LB
015	61	M/N	143	32	100
007	62	M/N	181	121	100
067	52	F /N	192	163	100 LB
049	75	M/N	213	169	200 LB
050	80	M/N	220	197	200 UB
036	64	M/N	261	238	100
064	54	F /N	262	188	300 LB
091	62	F /W	295	52	200
063	38	M/W	299	244	300 LB
066	63	M/N	327	203	200 LB
107	58	F/W	347	89	200
047	57	M/W	411	147	150 LB
111	52	F /N	434	307	200
062	60	M/N	451	270	150
096	42	M/N	583	439	100
113	72	F /N	632	381	100
098/103	45	F /N	912	474	200+300 LB
020	69	F /N	946	885	200
006	67	M/W	982	740	54
101	76	M/N	983	864	257 LB
100	76	M/N	1,258	900	300 LB
023	44	M/N	1,261	651	200
095/104	66	F /N	1,437	704	200+300 LB
108	66	F /W	1,691	584	300 UB

* Study No. refers to the roster of patients described serially in Technical Reports: No. 6–15[40], 18–29[41], 31–36[42], 6–64[43], 66–70[44], 77–82[45], 83–91[46], 92–103[47], 104–111[48], 112–113 personal communication.[ELS]

† Dose in rads at the midline. Where no letter follows the dose, whole body radiation was given. LB = lower body irradiation; UB = upper body irradiation. The dividing point is the xiphoid.

Median survival—327 days.

as far advanced and in a few instances as terminal. Four patients were not included in the study for medical reasons, or because the patients themselves declined participation in the study.

In order to make an appropriate comparison, several published series were reviewed. Series of cases of colon cancer metastatic to liver were utilized, since they were the best found by us with appropriate time periods of metastasis available for comparison. Stearns and Binkley,[51] in 32 patients with colon cancer with liver metastases, found a median survival time of 11 months after palliative resection of the primary tumor; in 28 of their patients in whom only biopsy or diversion was performed, the median survival was 8 months. In 353 patients with untreated colon cancer metastatic to liver, Pestana *et al.*[37] reported a median survival of 9 months. Figure 1 presents an analysis of 177 patients with liver metastases and no subsequent therapy reported by Jaffe *et al.*[20] There is also a group of 61 patients reported by Rapoport and Burleson[38] treated with 5-fluorouracil.

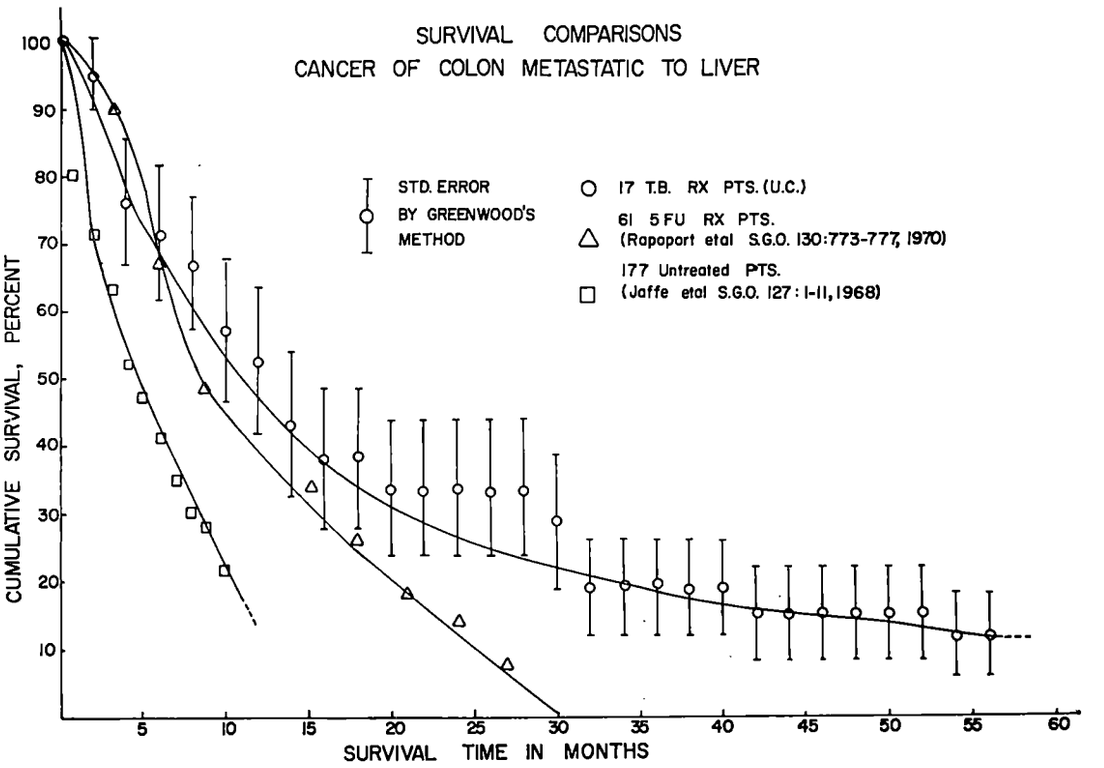


FIG. 1.

The 22 patients in our series with proven metastatic carcinoma of the colon to the liver treated by irradiation are also shown in Figure 1.

The median survival time for untreated patients was 146 days; for patients treated only with 5-fluorouracil, 255 days; and, among our patients with liver metastases, 391 days (Table II). A life table analysis was performed and indicates that the treatment given to our patients was approximately equivalent to the group given 5-fluorouracil. There was no evidence that the median survival time was shortened by total or partial body irradiation (Fig. 1). It should be appreciated that 5 of our patients had received or are receiving 5-fluorouracil in addition to the radiation therapy (3 of these with liver metastases).

The median survival for the entire group of 29 patients (22 with liver metastases) was 327 days.

CANCER OF THE BRONCHUS

This group of 15 patients (Table III) had far advanced disease with distant metastases at the time of treatment. The best comparison group was from our own institution reported by Horwitz *et al.*[16] The median survival of the 15 patients receiving whole body irradiation was 193 days from the time of diagnosis. The median survival of 61 patients seen at Cincinnati General Hospital from December, 1961, to June, 1964, was 135 days. In 15 of the 17 cases with distant metastases excluded by Horwitz *et al.* from their study (see caption to Fig. 2), the median survival was 32 days.

This last group of patients with distant metastases constitutes the most appropriate comparison group. When the median survival* of 15 patients mentioned by Horwitz *et al.*[16] is compared with the 15

* Two of the 17 patients excluded in the Horwitz *et al.*[16] study were treated by whole body radiation.

patients treated by whole body irradiation, the survival times are significantly different (Chi square 11.63, $p < 0.005$) (Fig. 3).

EWING'S TUMOR

This subgroup of 3 patients constituted the only one in which an attempt at curative therapy was made; all 3 patients are surviving. The times of survival are 854, 1,243 and 1,553 days from the time of diagnosis to August 31, 1972. The patient with the longest survival has recently developed a solitary pulmonary metastasis. The use of whole body irradiation to eliminate small clumps of cells in the disease has been reported by others.[21,33]

A fourth patient with Ewing's tumor had pulmonary metastases when first seen. Therapy in that case was only palliative.

TABLE II

CANCER OF COLON—CASES WITH METASTASES TO LIVER

(22 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)
106	40	25
109	116	80
052	120	91
033	126	86
082	136	33
015	143	121
067	192	163
036	261	238
091	295	52
066	327	203
107	347	89
111	434	307
062	451	270
096	583	439
113	632	381
098	912	474
006	982	740
101	983	864
100	1,258	900
023	1,261	651
095	1,437	704
108	1,691	584

* See footnote to Table 1.
Median survival—391 days.

TABLE III

LUNG CANCER—SURVIVAL IN DAYS AFTER D_x

(15 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)	Dose (rads)
053	57	28	200
056	103	38	100 UB
086	116	20	100
078	126	61	200
088	135	7	150
081	144	24	100
051	163	74	150
070	193	68	150
102	266	22	200 Trunk
018	333	298	200
044	349	196	100
011	419	323	100
112	683	403	100
025	797	33	150
084/097	855	643	300 UB+100

* See footnote to Table 1.
Median survival—193 days.

CANCER OF THE BREAST

In 15 cases treated by us the median survival from diagnosis to death was 479 days and after treatment to death was 446 days (Table IV). Two comparable reports in the literature include the one by the Committee on Estrogens and Androgens[52] and the other by Samp and Ansfield using 5-fluorouracil.[49] Again a life table analysis was done for our 15 patients and indicates that the survival of our patients appears somewhat better than that of the patients treated solely by estrogens and androgens, but not quite as good as the group treated with 5-fluorouracil (Fig. 4). The patients survive longer than those receiving the "standard therapy" as described by Samp and Ansfield;[49] this includes appropriate administration of estrogen and androgen, oophorectomy, local irradiation, adrenalectomy and hypophysectomy.

OTHER CANCERS

A remaining group of 25 cases reflected several different kinds of cancer. It is not

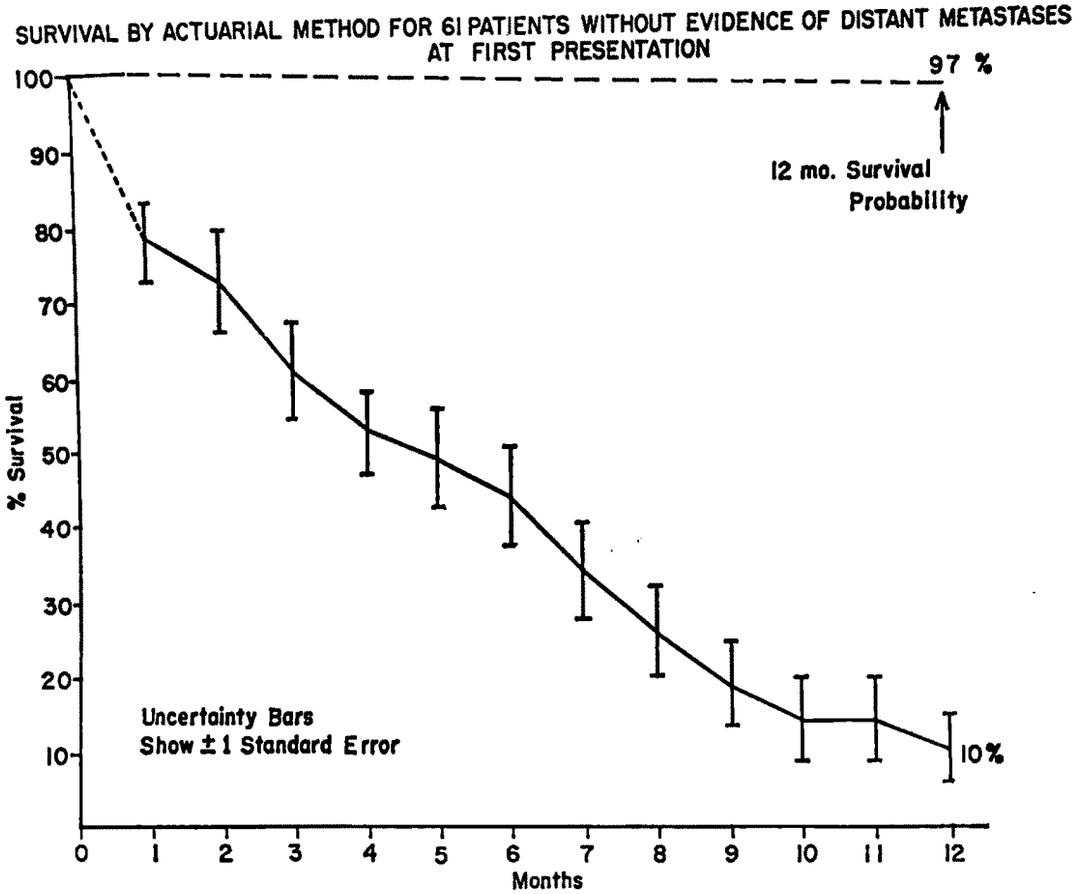


FIG. 2. The survival by actuarial analysis is shown for a total of 61 patients with carcinoma of the bronchus and distant metastases, who presented between December, 1961 and June, 1964 at Cincinnati General Hospital. The only patients excluded from this group are those in whom distant metastases were present at the time of diagnosis (17 patients). If they were to be included, the 1 year survival figure would drop to about 7 per cent. It is emphasized that these figures take account of all cases seen (including those apparently "early" and amenable to complete surgical resection). Although other reported figures may be somewhat higher, differences are more realistically attributable to biologic factors rather than to therapy.[16]

possible to make an analysis of these at this point since the individual case groups are too small to warrant this

DISCUSSION

RELATION OF RADIATION THERAPY TO PATIENT DEATH

Some analyses can be made which give information on this point.

The doses of whole body radiation given could initiate only the hematologic form of the acute radiation syndrome. In the healthy individual, after prodromal symptoms of malaise and vomiting lasting about 6–48 hours, there is a latent period lasting until 18–21 days after exposure. At this time there is a marked rapid fall in white blood cells and platelets and a less rapid fall of red blood cells reaching a nadir at 30–40 days and then recovering. These changes are associated frequently with episodes of infection and bleeding. Epilation will occur at doses over 300 rads.

Many of these patients had received much radiation and chemotherapy prior to total or partial body treatment and in

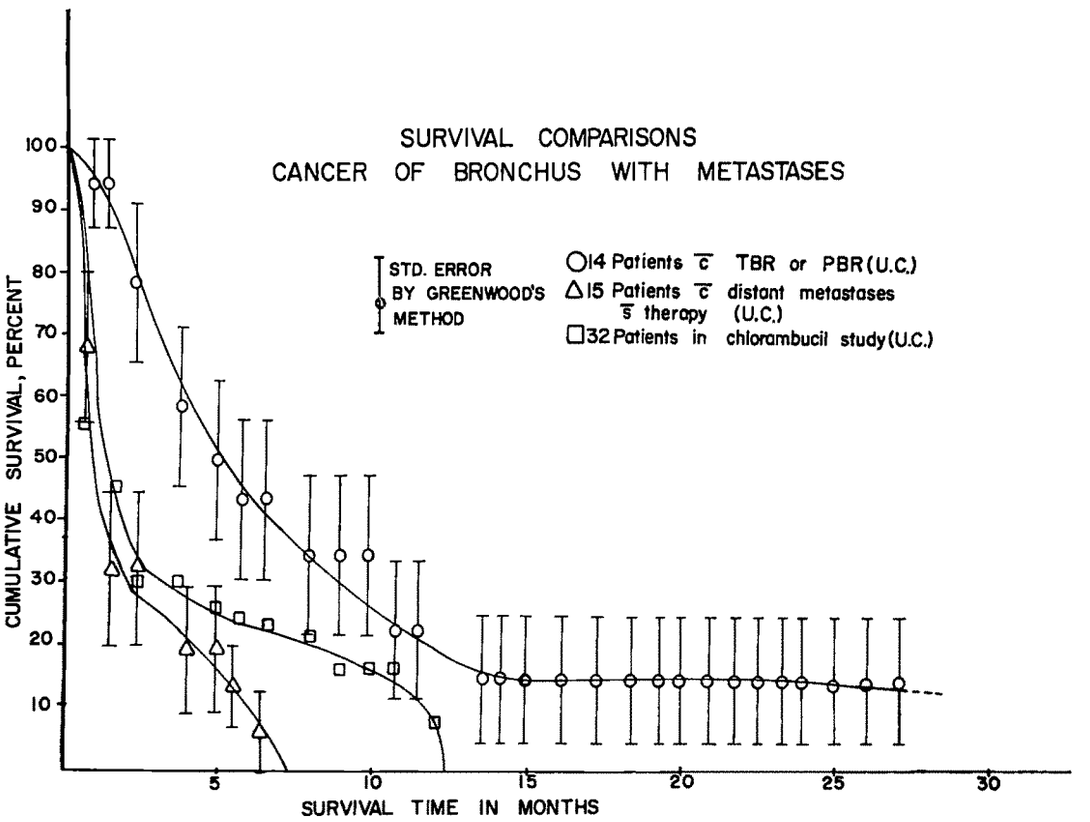


Fig. 3.

many cases this treatment was followed immediately by planned local therapy to various portions of the body.

If one assumes that all severe drops in blood cell count and all instances of hypocellular or acellular marrow at death were due only to radiation and not influenced by the type or extent of cancer and effects of previous therapy, then one can identify 8 cases in which there is a possibility of the therapy contributing to mortality. Of this subgroup, 2 patients received localized radiation between total body irradiation and death at 31 and 32 days, respectively. Two had extensive previous chemotherapy and 1 also had local radiotherapy. In 2 other cases, autologous marrow transfusion was unsuccessful because the preradiation marrow was hypocellular. Both of these latter patients had had intensive localized irradiation and 1 had received intensive chemotherapy.

Table IV

CANCER OF BREAST—SURVIVAL POST D_x

(15 Patients)

Study No.*	Survival After D_x (days)	Survival After R_x (days)	Dose (rads)
089	101	16	200 Trunk
055	175	156	200 UB
029	285	152	150
060	316	30	150
045	138	25	150
022	473	10	150
094	473	354	150 Trunk
031	479	446	100
079	554	209	100
010	783	48	100
008	1,056	91	100
035	1,068	859	150
040	1,095	1,063	100
083	1,098	264	100
092	1,308	1,143	150 Trunk

* See footnote to Table 1.
Median survival—479 days.

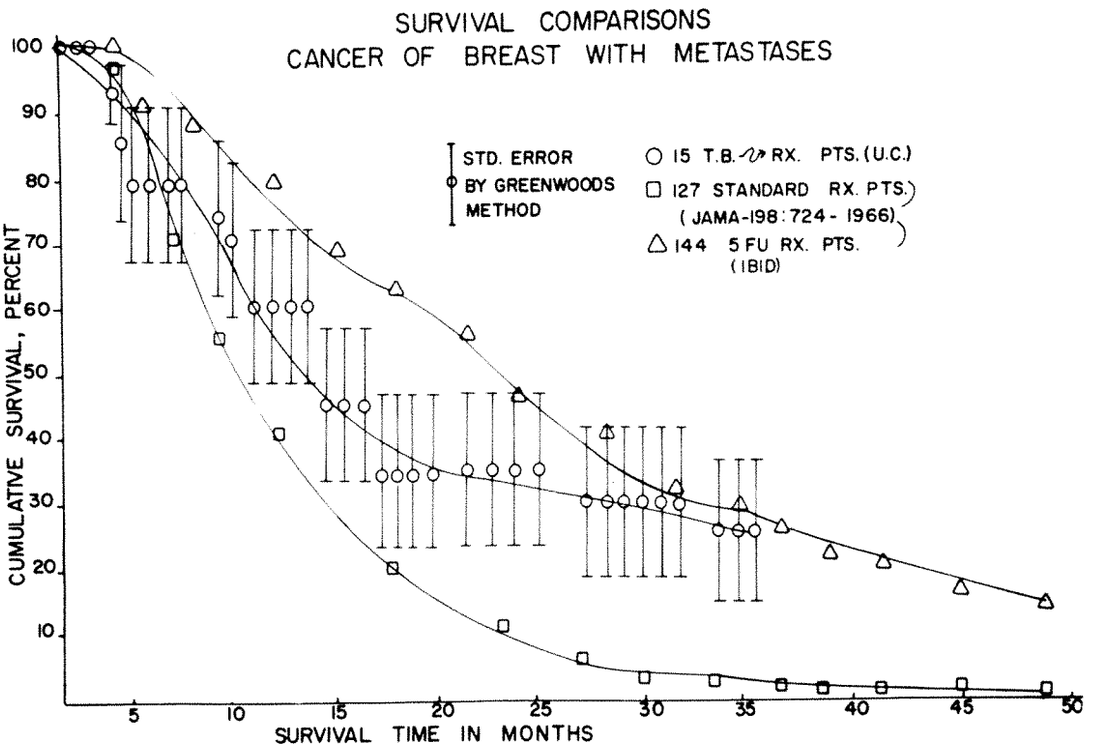


FIG. 4.

Of the 19 patients who died within 20–60 days, 11 showed clear evidence of well functioning marrow with steady or rising white blood cell counts and absence of bleeding and infection at the time of death.

The time from diagnosis to death of the 24 patients entered in the study who were not treated has been analyzed. There were 4 who died in a 20–60 day interval:

	No. of deaths in 20–60 days	*Patients surviving or dying at other times*	*Total*
Patients not given radiation	4	20	24
Patients given radiation	19	63	82

Fisher's exact probability test yields a p value of 0.16, indicating that there is no difference between the 2 groups. Therefore one may conclude that in other patients described, the effect of whole and partial body radiation therapy was less important in contributing to death than was the extent of disease in these patients. Another interpretation would be that a physician selecting far advanced cancer patients for a given treatment would have about the same degree of difficulty in selecting any form of treatment for these very ill patients. The same probabilities, $p = 0.19$, 0.2 and 0.21 are found for patients dying between 0 and 20 days post treatment, from 0–60 days, and from 20–40 days, when compared to the untreated group. Current status of survival for these 88 treated patients is as follows:

Prophylactic therapy (Ewing's tumor)	3
Others surviving as of August 31, 1972	7
Deaths possibly attributable to irradiation	8
Deaths attributable to tumor	70
	88

REACTIONS FROM TREATMENT AND EFFECTS OF PALLIATION

The acute radiation syndrome develops in stages. In the prodromal stage, nausea and vomiting of a transient nature occur.

These complaints are often highly subjective; therefore, they are not discussed with the patient before treatment.

The analysis of our 88 treated patients shows that 44 per cent experienced no symptoms at all, that 27 per cent had transient nausea and vomiting within 3 hours, 14 per cent within 6 hours and 3 per cent within 12 hours. In only 4 patients (4 per cent) were the nausea and vomiting of a severe nature (Table v).

These symptoms are no greater than found after surgery or after treatment with cancer chemotherapy drugs, the reactions of which are often far more severe than those from these kinds of radiation therapy. Lahiri *et al.*[29] observed that when 5-fluorouracil is given orally at a dose of 15 mg./kg. daily for 6 days, and then weekly at the same dose, nausea, vomiting, diarrhea or stomatitis are found in 55 per cent of the patients treated, and marrow depression is observed in 50 per cent. A recent study by the Western Cooperative Cancer Chemotherapy Group, employing 5-fluorouracil without a loading dose at 15 mg./kg./wk. for a month, reported mild to major gastrointestinal or hematologic toxicity in 85.5 per cent of 430 patients.[17] Higgins *et al.*[12] in treating cancer of the colon using 12 mg./kg. of 5-fluorouracil intravenously for 5 successive days, observed that 27.9 per cent of 359 patients experienced a toxic reaction. The same group reported one or more surgical complications following resection of colon carcinoma in 29.6 per cent of 433 patients. Parsons *et al.*[35] note that 61–72 per cent of patients suffering from so-called radiation sickness responded favorably to placebo medication, indicating that suggestibility may have a big part to play in the appearance and control of these symptoms. Mukherji *et al.*[34] in evaluating the effectiveness of a combination of 4 drugs in the treatment of 23 patients with lymphosarcoma and reticulum cell sarcoma found severe myelosuppression in 4 patients (17 per cent) and possibly attributed this depression to their deaths from infection.

During the latent period of 18–21 days the patient is asymptomatic. The period of manifest illness then begins with evidence of malaise, infection and bleeding. These findings occur only with whole body irradiation and not with partial body treatment. Also when marrow is successfully replaced these findings do not occur.

Table V

INCIDENCE OF NAUSEA AND VOMITING IN 88 CANCER PATIENTS RECEIVING WHOLE AND/OR PARTIAL BODY RADIATION THERAPY

	Patients	Per Cent
No nausea or vomiting	39	44
Nausea and/or vomiting up to 3 hours after R_x	23	27
Nausea and/or vomiting up to 6 hours after R_x	12	14
Nausea and/or vomiting up to 12 hours after R_x	3	3
Nausea and/or vomiting up to 24 hours after R_x	7	8
Nausea and/or vomiting up to 48 hours after R_x	0	—
Nausea and/or vomiting 48 hours +	4	4
	88	100

In regard to palliation, a review of patient records shows that some palliation was achieved in 56 per cent and that 31 per cent were made neither better nor worse (Table vi). In another 3 cases we were unable to obtain follow-up history concerning palliative effects. The 3 cases of Ewing's tumor are not included in this table as therapy was prophylactic.

POSSIBLE UNIQUE MECHANISMS OF WHOLE AND PARTIAL BODY IRRADIATION

Whole body irradiation in the doses reported herein could be effective against cancer in several ways: (1) alteration of the immune mechanism of the body altering the balance in favor of the host; (2) by a direct effect on the metabolism of the cancer cells. In this case wide-field radiotherapy would have one advantage over drug therapy, since it would reach all cancer cells without depending upon blood

TABLE VI

PALLIATIVE EFFECTS* OF TREATMENT

(85 Patients†)

	Per Cent
Relief of pain	31
Decrease in tumor size	31
Increase in activity	13
Increase in well being (weight gain, appetite improvement, subjective statement by patient)	30
One or more of the above	56
No change	31
Lost to follow-up for evaluation of palliation	4
Death between 20 and 60 days possibly attributable to radiation	9

* In some of the patients there was more than one indication of improvement; thus, the percentages exceed 100 per cent.

† 3 children with Ewing's tumor received prophylactic treatment and are not included in this analysis.

supply, or chemical and pharmacologic distribution.

Partial body irradiation could be compared to regional isolation perfusion with antineoplastic drugs, again being certain to reach all tumor cells within the irradiated volume and lacking the more hazardous systemic effects of total body irradiation.

The effectiveness of both methods may be explained by the fact that small tumor foci are more sensitive to treatment than large foci and that single cancer cells are more susceptible than clumps of cells.

PSYCHOLOGIC AND PSYCHIATRIC EVALUATION OF PATIENTS

A unique and important aspect of the research work in this project has been the attempt to evaluate and distinguish between the manifestations of cancer and the effects of radiation therapy in regard to psychologic and psychiatric changes. For example, others have reported on personality types in certain cancers,[2] but no studies were presented investigating the effects of treatment.

In 1969, we reported on the effect of total and partial body irradiation on the cognitive and emotional processes of 16 patients.[11] This number has been increased to 43. These studies consisted of administration of a battery of tests to each patient in the pretreatment phase, during sham and actual treatment and during a 6 week post-treatment period. Tests which have been utilized included the Halstead Battery, Wechsler-Bellevue Adult Intelligence Scale, some tests of intellectual impairment modified from Reitan, and the 5 minute verbal content test of Gottschalk and Gleser. There has been some change in the several tests which we have been using during this phase of the total project; *i.e.*, not all tests have been used continually.

In the baseline data of 39 patients tested, the median intelligence quotient was 87 and the mean also 87. There were 41 per cent of subjects with I.Q. values of 95–116, 47 per cent between 71–95, and 12 per cent between 63–70. The distribution of intelligence factors as measured by several tests is representative of the population served by the General Hospital.

It is clear that the intensive study and the above testing have had a helpful effect in increasing the level of motivation to cooperate, as exhibited by all patients so studied.

The need for careful handling of the cancer patient by all members of the medical team is emphasized by the consistent evidence of depression over the 7 week study period. The depression is lessened with clinical improvement and attention to patient needs. It is also less in patients with long survival (over 100 days) as would be expected. Similarly, hope is directly related to survival. Anxiety dips sharply during sham treatment; it increases just prior to actual treatment, then decreases and levels off. Outward hostility tends to increase at the time of post sham treatment, then dips and remains quite stable. Hope as measured by the content analysis of verbal behavior is related to satisfactory human relations in the patient's life situation.

USE OF AUTOLOGOUS BONE MARROW TRANSPLANTATION

Because of radiation-induced hematologic depression, autologous bone marrow storage and reinfusion were instituted in 1964. Employing the method of Kurnick,[28] marrow was removed from the posterior iliac crest under local anesthesia, to an average value approximating 300 cc. It was mixed with Osgood-glycerol medium and stored at −83° C. following a programmed temperature reduction of 1° C. per minute. Prior to reinfusion dextrose was added, and then the marrow was given intravenously, initially without filtration, at a rate of 50 to 60 cc. per minute. The first 2 patients who received a marrow transfusion in our study, Patients 051 and 053, were infused with frozen marrow 24 and 19 days post irradiation, respectively, at a time when the marrow sinusoids were relatively empty of precursor cells, with the expectation that there would be more room for the transplant to take. Marrow viability in these 2 procedures was 55 and 57 per cent.[45]

Patient 051 experienced moderate hemoglobinuria not seen in Patient 053 after infusion. Marrow was given in both cases 2 to 3 weeks post irradiation; hence, it was impossible to distinguish spontaneous marrow recovery from successful marrow autotransfusion.

Because hemoglobinuria had been noted, a triple filter system was developed and marrow autotransplantations on Patients 070, 077, 078, 087, 090, 091, 095, 098, 099, 107 and 111 have all been performed employing this filter system.[48]

In marrow transplants of Patients 070, 077, and 078, the delay between the removal of marrow and transfusion was 11, 2 and 0 days, respectively. The platelet count of Patient 078 never fell below 125,000 per mm.^{3}, but the white blood cell count dropped as low as 900, suggesting possible effectiveness of the technique for the first time.

For the next 8 patients the technique was therefore modified, so that a larger volume of marrow (500 cc.) was removed from the patient under general anesthesia. The patient was then irradiated and the marrow replaced intravenously on the same day as it was removed. The results in Table VII indicate the success attendant on the modification of this procedure. Five patients receiving 200 rads of whole body radiation showed mean white blood counts to be 2,820 ± 804 cells per mm.^{3} at the nadir. In 7 patients given the same dose but no autograft, the level at the nadir was 850 ±380 cells per mm.^{3}, the 2 means being significantly different (Table VIII). The first patient transplanted with our new technique (Patient 087) was followed in the Clinical Research Center, Cincinnati Children's Hospital, for over 6 weeks without any evidence of illness. Subsequently patients receiving these whole body doses have only been hospitalized for a total of 5 days or less. The degree of marrow depression in the successfully transplanted patient is such that hemorrhage and infection are not observed.

The 3 failures in the revised transplantation technique have been Patient 090, 099 and 107. Patient 090 suffered a cerebrovascular accident unrelated to her tumor or her radiotherapy. The latter 2 patients (099, 107) had had widespread radiotherapy which had affected the reticuloendothelial framework necessary for stem cell development, and preliminary cell aspirates in allegedly unirradiated areas did appear hypocellular. Patient 107 appeared to possess normal granulocyte reserves, one of our marrow screening parameters, only because we were given an incorrectly high body weight on which to base our etiocholanolone dosage, thus falsely elevating the marrow granulocyte reserves. From this unfortunate experience we now insist that a candidate for marrow autotransplantation have a normal iliac marrow aspirate histologically, a normal bone marrow scan employing technetium 99m sulfur colloid, and normal granulocyte reserves measured with etiocholanolone (after we weigh the patient) as indicators of normal marrow function. At autopsy, Pa-

TABLE VII

WHOLE BODY IRRADIATION WITH MARROW TRANSPLANTATION

Study No.*	Type of Transplant	Whole Body Dose (rads)	Date of Marrow Removed	Date of R_x	Date of Marrow Reinfused	No. of Cells Reinfused	Viability	Marrow Frozen	Complications of Infusion	Outcome of Autograft
051	Auto	150	4/26/65	5/1/65	5/25/65	1.6×10^9	55%	Yes	†Hemoglobinuria for 1 day	Did not take
053	Auto	200	5/ 4/65	5/ 8/65	5/27/65	1.4×10^8	57%	Yes	†None	Did not take
070	Auto	150	5/ 4/65	3/ 2/67	3/13/67	0.33×10^8	68%	Yes	None	Did not take
077	Auto	200	10/31/67	11/ 7/67	11/ 9/67	0.79×10^8	48%	Yes	Hemoglobinuria for 12 hours	Did not take
078	Auto	200	11/ 4/67	12/ 5/67	12/ 5/67	4.16×10^9	96%	No	None	Possible partial take with platelets never below 125,000/mm.^{3} but leukocytes 900/mm.^{3}
087	Iso	200	3/ 3/69	2/27/69	3/ 3/69	4.38×10^9	99%	No	None	Take
090	Auto	150	2/ 2/69	2/ 2/69	2/ 2/69	15.6×10^9	96%	No	None	Cerebrovascular accident killed patient 6th day after R_x
091	Auto	200	7/ 2/69	7/ 2/69	7/ 2/69	4.6×10^9	98%	No	None	Take
095	Auto	200	11/ 5/69	11/ 5/69	11/ 5/69	3.07×10^9	97%	No	None	Take
098	Auto	200	1/27/70	1/27/70	1/27/70	7.42×10^8	98%	No	Transient hypotension before infusion	Take
099	Auto	230	3/ 3/70	3/ 3/70	3/ 3/70	5.32×10^9	95%	No	None	No take
107	Auto	200	12/15/70	12/15/70	12/15/70	3.2×10^9	95%	No	None	Take doubtful-leukopenia but no sepsis
111	Auto	200	5/19/71	5/19/71	5/19/71	7.4×10^9	96%	No	None	Take

* See footnote to Table 1.
† Unfiltered marrow infused.

TABLE VIII

RESULTS OF SUCCESSFUL ISO- AND AUTOTRANSPLANTS OF MARROW AFTER 200 RADS MIDLINE WHOLE BODY IRRADIATION

Study No.	Day of Leukocyte Nadir	Leukocyte Count at Nadir (cells/mm.^{3})	Nucleated Cell Count Infused Per Kilogram Body Weight‡
087	26	2,100	1.6×10^8
091	25	4,100	2.3×10^8
095	33	2,700	0.6×10^8
098	28	2,200	1.7×10^8
111	31	3,000	1.4×10^8
Mean	28.6	$2,820\pm804$†	1.5×10^8
Mean of Controls*	24	850 ± 380†	—

* 7 patients receiving 200 rads whole body radiation without transplantation of marrow.
† The means differ significantly by the t test at $p<0.001$ and by the Wilcoxon two sample test at $p<0.02$.
‡ It has been estimated that 1.1×10^7 cells/kg. are required for a successful marrow iso- or autotransplant.[48]

tient 099, who died on Day 31 post irradiation, had widespread carcinoma of the pancreas. Patient 107 survived her pancytopenia without any evidence of sepsis. Patient 111 had no significant cytopenia and her hospitalization (including autotransplant) lasted only 4 days.

This technique has been of advantage in simplifying the patient's course and eliminating the long period of hospitalization needed prior to transfusion. The possibility of reinfusing tumor cells in the untreated marrow exists, but the elimination of this problem awaits the development of successful methods of marrow allotransplantation.

SUMMARY

1. Whole and/or partial body radiation therapy given in single doses has shown beneficial effects in the control of certain advanced cancers. The palliative effects compare favorably with results using anticancer drugs as commonly reported in the medical literature.

Irradiation certainly seems to improve survival in the untreated patient with cancers of colon, lung and breast.

2. The use of autologous marrow reinfusion immediately after radiation therapy minimizes the characteristic marrow depression otherwise observed. The degree of illness following infusion is greatly lessened and hospitalization greatly shortened.

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VALUE OF MAMMOGRAPHY IN REDUCTION OF MORTALITY FROM BREAST CANCER IN MASS SCREENING*

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THE one-third reduction in mortality rate from breast cancer achieved in the mass screening program of the Health Insurance Plan of Greater New York, under contract with the National Institutes of Health, has persisted in a 5 year follow-up. The important role of mammography in this reduction is pointed out by the fact that of 44 cancers found on mammography alone in this study only 1 woman has died in this period.

BACKGROUND

Since 1963 the mass screening program for breast cancer detection has been conducted by the Health Insurance Plan of Greater New York under contract with the National Institutes of Health. The project was stimulated by the fact that the death rate from breast cancer in the United States has remained stationary for 35 years in spite of surgical, radiotherapeutic and chemotherapeutic advances. Because there is a substantially increased survival in breast cancer cases with no axillary lymph node involvement, it was felt that there was a potential for lowering the death rate through earlier detection. The concept was also abetted by the introduction of the newer method for mammography introduced by Egan.[1]

Limited breast cancer screening programs by Gershon-Cohen *et al.*,[2] Witten and Thurber,[5] Stevens and Weigen,[4] and Wolfe[6] have indicated the feasibility and potential of such projects. It was thus considered that a mass screening program using both clinical examination and mammography might lead to substantially increased detection of localized cases and thus perhaps to a lowering of the death rate. Such a screening program also offered the possibility of evaluating the role and special importance of mammography.

PROCEDURE

A group of 62,000 women aged 40 to 64 years were chosen at random from the members of the Health Insurance Plan medical groups. Those with a history of previous breast cancer or who were pregnant at time of examination were not included. The women were carefully chosen as 31,000 matched pairs. One set was designated as the study group and the other as the control group. Of the study group women who were invited to participate 65 per cent responded and were examined with independent clinical examination and mammography. The nonresponders were followed through records as study group, not examined. The control group women received their usual comprehensive medical care at their groups, but were not screened in the program. Their breast cancer history was followed through records at central headquarters.

Study group women who responded were offered an initial and 3 subsequent annual examinations. Clinical examination was performed by a member of the group to which the women belonged, usually a surgeon. The examination was conducted without knowledge of the roentgenographic

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findings. Mammography was performed with the Egan technique including use of industrial fine-grain film (type M), low kilovoltage, long and variable target-film distance and close coning. Cephalocaudad and mediolateral views of each breast were obtained. The radiation dosage to skin averaged 7.7 rads. All films were read by 2 radiologists without knowledge of clinical findings.

About 20,000 women or 65 per cent of the study group received the initial screening examination. Of these on subsequent annual re-examination, 80 per cent responded for their first annual, 74 per cent for their second and 69 per cent for their third. About 60 per cent of the screenees received all 4 examinations. All screening examinations have been completed.[3]

TABLE I

BREAST CANCER DETECTION RATES
5 YEARS OF OBSERVATION FROM DATE OF ENTRY

Population	Breast Cancers	
	No.	Rate per 1,000*
Study-screened		
Detection due to initial examination†	55	2.72
Detection due to annual re-examination	77	1.51
Detection not due to screening‡	91	0.92
Study-refused screening	73	1.37
Control	284	1.86

* 20,211 women had initial screening examination.
† Includes only cases diagnosed in course of regular medical care; case detection not due to follow-up of screening findings.
‡ Rate of detection due to initial screening is per 1,000 women examined; other rates are per 1,000 person-years.

FINDINGS

In the study group, 296 breast cancers were found compared to 284 in the control group. The prevalence rate on initial examination of breast cancer in women who were screened was 2.72 per 1,000. The detection rate in subsequent screening was 1.51 per 1,000 person-years. Cancers were detected in screened women after a negative examination anywhere from 2 months to almost 5 years at a rate of 0.92 per 1,000 person-years. Incidence rate among study group women who refused screening was 1.37 per 1,000 and in the control group 1.86 per 1,000 (Table I). The low rate of the study group not examined suggests that study women tended to self-select themselves for screening.

Mammography contributed substantially to the yield. Of 132 breast cancers detected through screening, 44 or 33 per cent were found on mammography only and would have been missed if this modality were omitted. At the same time, 59 cancers or 44 per cent would have been missed if clinical examination were not included. However, in women under 50, whose breasts tend to be smaller and more glandular, only 19 per cent of the cancers would have been missed without mammography and 61 per cent would not have been detected without clinical examination. In women over 50, the two modalities made similar contribution to cancer detection (Table II).

Over-all, no axillary lymph node involvement was found in 70 per cent of screened women. In the mammography only group, 77 per cent were free of lymph node involvement. The figure for the clinical only group was 76 per cent. This compares with 46 per cent for the control group. For the total group of study women (including those whose cancers were not detected as a result of screening) no lymph node involvement was found in 57 per cent (Fig. 1).

MORTALITY

Direct comparison of deaths from breast cancer in the study and control groups corresponds to mortality rates, since the 2 groups were random selections of equal size, carefully matched and set in defined time periods.

In a 5 year follow-up period, 63 deaths from breast cancer occurred in the control group compared to 40 in the study group—only two-thirds of whom were actually screened (Fig. 2). In the first 2 years of

TABLE II

BREAST CANCERS DETECTED ON SCREENING BY AGE GROUP AND MODALITY

Modality*	Total	Age at Diagnosis		
		40–49	50–59	60 or Older
		Number		
Total	132	31	65	36
Mammography only	44	6	27	11
Clinical only	59	19	26	14
Clinical and mammography	29	6	12	11
		Per Cent†		
Total	100.0	100.0	100.0	100.0
Mammography only	33.3	19.4	41.5	30.6
Clinical only	44.7	61.3	40.0	38.9
Clinical and mammography	22.0	19.4	18.5	30.6

* Initial evidence for biopsy recommendation made independently by the 2 modalities.
† Percentages in this table may not add to 100 due to rounding.

follow-up, breast cancer mortality was similar in the 2 groups. In subsequent years, women in the study group had a substantially lower death rate. However, the lower breast cancer death rate is noted in women over the age of 50 years. The death rates are almost the same in those under 50 years.

Another measure of breast cancer mortality is to examine the probabilities of death among women with confirmed breast cancer during specified periods following diagnosis—the case fatality rates. These rates include deaths among breast cancer women regardless of cause of death and are calculated separately for the control group cases and for the subcategories of cases in the study group. Allowance in these tables is made for the lead time in diagnosing breast cancer gained by the screening program. This lead time is estimated to be about 1 year. The 5 year case fatality rate is substantially higher in the control group than in the study group: 42 *vs.* 28 per cent. The rate among study women who refused screening is 35 per cent. When the rate is restricted to the 132 breast cancers detected through screening, the rate drops to 17 per cent, with only 1 death occurring thus far among the 44 breast cancers detected through mammography alone (Fig. 3). In the other 88 cases of cancer detected through screening, 16 deaths have occurred, 10 of which were detected by the clinician only and 6 by both clinician and radiologist. Thus, while both modalities contributed to the improved case fatality rate, mammography was of particular importance in this regard.

Breakdown of case fatality rate by age groups revealed that no reduction of mortality was produced in the 40 to 50 year age group—all the gain was concentrated in those over 50.

SUMMARY

A randomized mass screening program using mammography as well as clinical

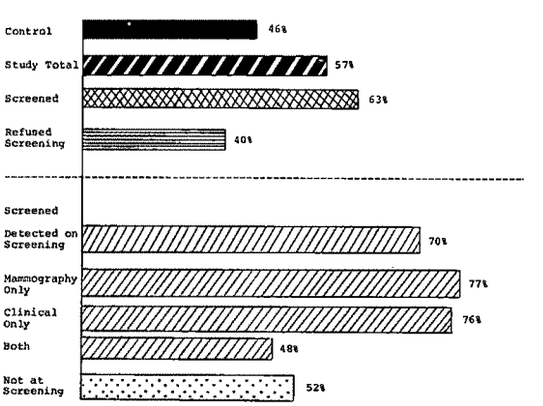


FIG. 1. Per cent of breast cancers with no histologic evidence of axillary lymph node involvement.

examination in women aged 40 to 64 years resulted in a higher proportion of breast cancer detected with no axillary lymph node involvement and subsequently a substantial reduction in mortality in a study group as compared to a matched control. Both clinical examination and mammography contributed independently to the yield. However, in women under 50 in this study, mammography led to detection of only a small proportion of additional cases, while at age 50 years and over omission of either modality would have led to substantially lower cancer detection rates. The particularly substantial contribution of mammography is underscored by a case fatality rate of only 2 per cent in cancers detected in mammography alone.

It would be reasonable to conclude that further follow-up to determine long-term effect of the screening procedures is indicated.

It would also seem useful to evaluate the contribution of newer improved methods of mammography and introduction of other modalities such as thermography in improving results in women under 50 years of age.

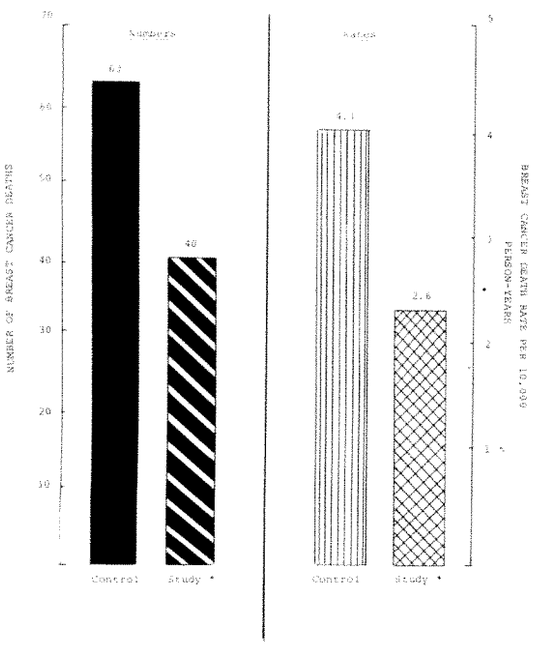


Fig. 2. Deaths due to breast cancer, 5 years of follow-up after entry to study.

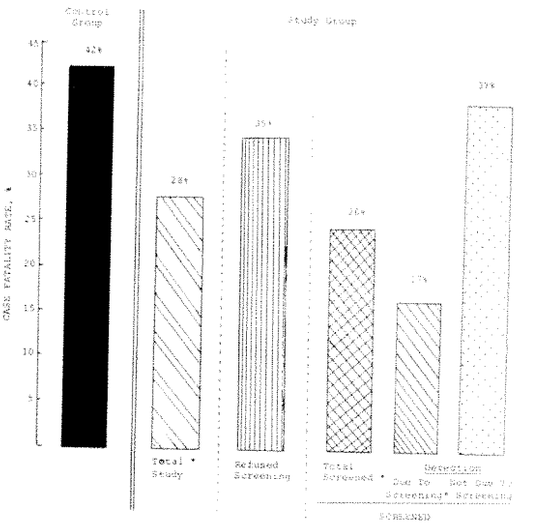


Fig. 3. Five year fatality rates among breast cancer cases.

* Allowance made for 1 year lead time in cancer detection due to screening.

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XERORADIOGRAPHY: IMAGE CONTENT AND COMPARISON WITH FILM ROENTGENOGRAMS*

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XERORADIOGRAPHY is an electrostatic imaging system based on the photoconductor selenium. It is an application of the xerographic process first discovered by Chester Carlson in 1938.

This article discusses contrast and recording latitude of the xeroradiographic image (XR) and compares it to those of silver halide roentgenograms.

The reader is referred to previous publications for a more complete discussion of the science of xerography, xeroradiography in previous medical publications.[1–11] Suffice it to say in this paper, that xeroradiography is an x-ray imaging process which uses a photoconductive plate, electrostatic charges and xerographic type processing. The xeroradiographic plate upon which the image is formed has an aluminum base which is coated with a thin photoconductive layer of vitreous selenium. The plate is held in a cassette which protects the plate from exposure to ambient light and surface damage. The steps in the xeroradiographic process are as follows: The XR plate is charged to a high positive potential by corona discharge, it is then placed in a cassette and used in a manner similar to that with conventional film in its cassette. When x rays strike the selenium, photoconduction occurs and this produces a charge image of the part examined. The image is made visible by bringing into proximity to the plate charged developer or toner particles. The resultant powder image is subsequently transferred to paper and fused providing an opaque XR for interpretation and storage.

The discussion is limited to non-mammographic applications. It is further concerned with the "negative XR" as opposed to the positive one which was used exclusively by early investigators and is now utilized for mammography. A negative XR refers to the tonal relationships and they are the same as those of x-ray film; exposed areas are dark blue (film—black) and unexposed areas are white (film—clear). The opposite exists in the positive XR.

This study leads one to conclude that both recording systems with proper radiographic exposure factors record similar information, but present it to the interpreter in differing forms as to degrees of contrast and latitude.

CONTRAST

A stepped wedge provides an excellent vehicle for discussing image contrast (Fig. 1).* From the figure and accompanying densitometer tracings, it is apparent that there are 2 types of XR image contrast: that which occurs at the step and it is great (edge enhancement); and that which exists between the flat portion of the steps themselves and is more subtle (broad area contrast). The XR image is a combination of these contrasts which are manipulated by externally applied electrodes, electric fields, time and amount of developer used to give the desired results.

The XR edge enhancement phenomenon

* A short explanatory note and qualifications of the Figures are as follows: The radiographic factors chosen for the stepped wedge images are intentional and intended to be comparable technique for a small extremity; *i.e.*, in xeroradiography of small extremities a relatively high kvp. is always used (120 kvp. or more). The 30 mas. represents that amount of radiation required for anteroposterior examination of the ankle. On the other hand, the 60 kvp. and 5 mas. utilized in the production of the stepped wedge image on x-ray film represents a practical technique. The author believes that it would be unrealistic to match the techniques for the purpose of a stepped wedge comparison because one cannot match techniques in everyday practice and obtain optimum images.

In the subsequent illustrations, where comparisons are made between an XR and a film roentgenogram of the same part, the reader should realize that XRs lend themselves to photography and reproduction better than the usual film roentgenogram. Therefore, the side by side visual comparison reproductions are somewhat limited in value.

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is due to the effect of fringing electric fields that occur at discontinuities in density and is proportional to the sharpness and degree of change in the voltage pattern that exists on the selenium plate after x-ray exposure; *i.e.*, if the change in object density is abrupt and great, the degree of edge enhancement of the image is correspondingly greater than if the change were less sharp or the object had a smaller "step."

Note that the density differences at the step are exaggerated in 2 ways: (1) there is an increased deposition of the development powder (toner) above the density of the plateau representing the thicker step; and (2) immediately after that there is significantly less toner deposited than on the plateau of the thinner step. The broad areas of the steps have considerably less density differences between them than the edges. The step wedge examples depict well the differences between an XR image and an x-ray film. With x-ray film there is no edge enhancement, but the density difference representing the steps (broad area) is greater on the x-ray film than on the XR (Fig. 2).

The value of edge enhancement is well exemplified by a fracture (Fig. 3, *A* and *B*). The fracture represents a sharp break in object density on a broad uniform area and the XR records it in exaggerated contrast. The x-ray film also shows the abnormality but usually not as well. A similar situation exists in other fractures such as in the skull. The XR is especially good, where there are multiple overlapping structures such as in the ankle or elbow.

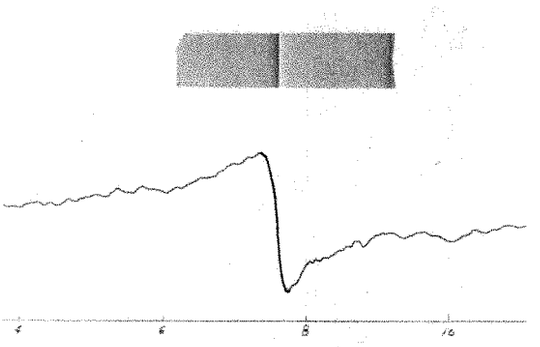


Fig. 1. XR (xeroradiograph) of stepped wedge (120 kvp., 30 mas., 36 inch, nongrid exposure). The edge enhancement is noted by the upward deflection of density most apparent at 6.7 and peaking downward at 6.9. The contrast gradient is much greater than that between the plateaus (approximately 0.6 units of reflectance *vs.* 0.1 for the broad area).

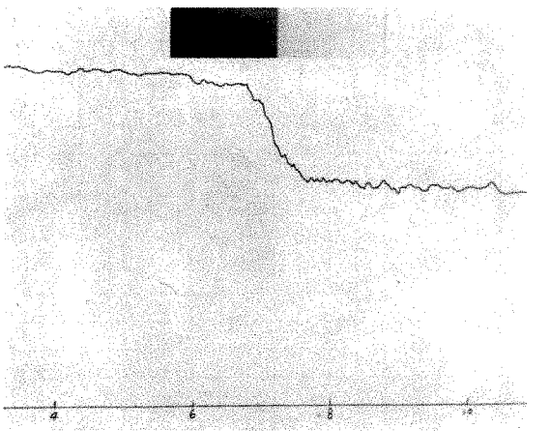


Fig. 2. Film roentgenogram of stepped wedge (69 kvp., 5 mas., 36 inch, nongrid exposure). There is no edge enhancement but the contrast gradient between the 2 broad areas of the steps is almost 0.4 units of transmission.

Differences in density over broad areas, especially when the gradation is slight, are usually shown in greater contrast with the x-ray film, although the information is recorded on the XR in a different form. Often, however, within the density of the abnormal area there is more information on the XR due to a combination of its better latitude and the edge enhancement phenomenon. It is to be stressed that the same amount of information can be gotten on the x-ray film with multiple images of varying roentgenographic exposure factors (Fig. 4, *A* and *B*; and 5, *A* and *B*).

RECORDING LATITUDE

The varying densities of structures recorded on an XR are routinely greater than those which are obtained on the usual "good technique" x-ray film. This feature of xeroradiography is well exemplified by the degree of soft tissue visualization obtained when properly exposing a part for osseous

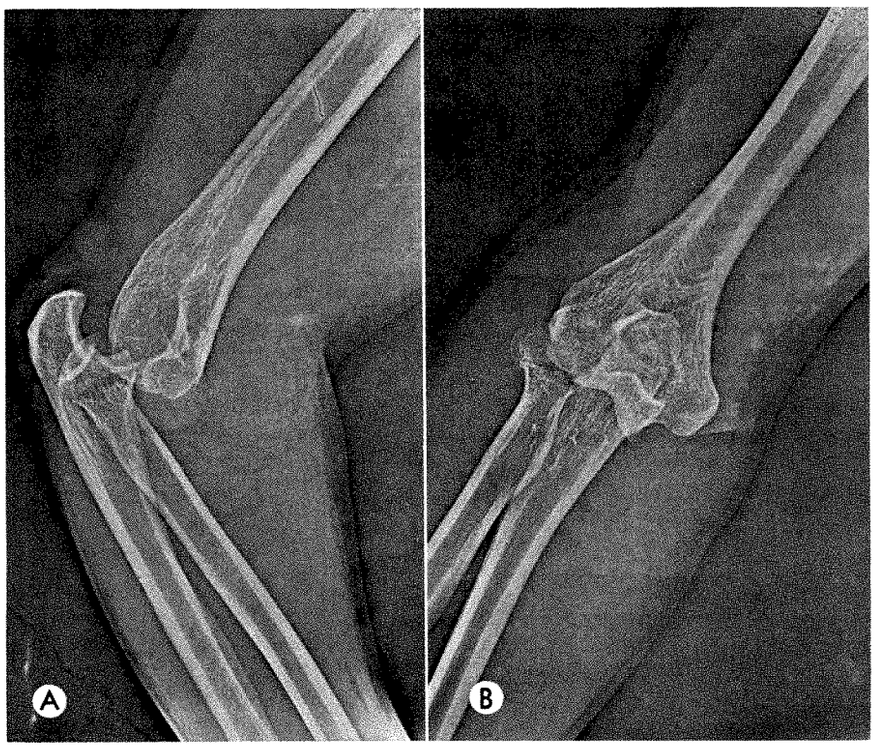


FIG. 3. (*A* and *B*) Fracture and dislocation about elbow. The radius and ulna are dislocated posteriorly. Note also a fracture of the radius. The relationship of the bones can be judged a little better on the antero-posterior XR than on the usual film image.

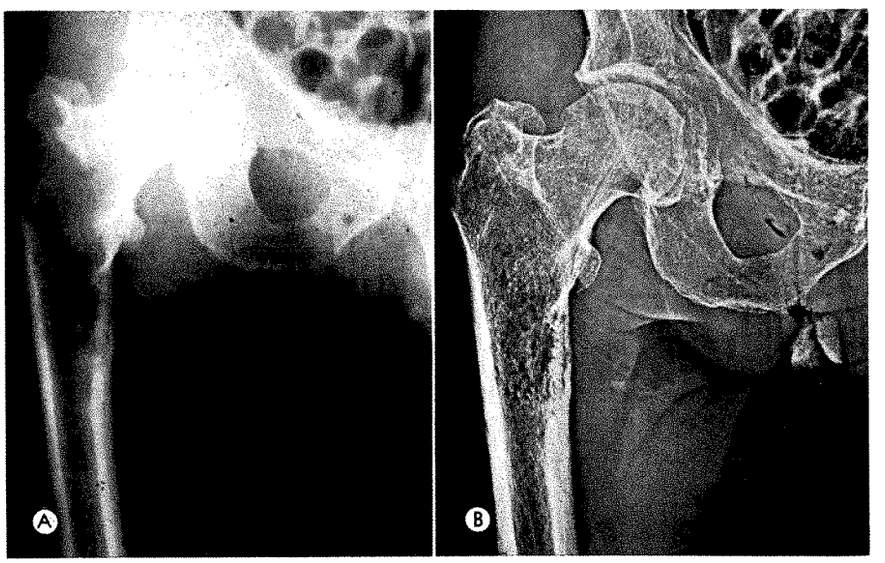


FIG. 4. (*A* and *B*) Metastasis to femur from bronchogenic carcinoma. Note that the "lucency" of the destructive lesion is more apparent on the film image (*A*), whereas more of the over and underlying details of the abnormal area are seen on the XR (*B*).

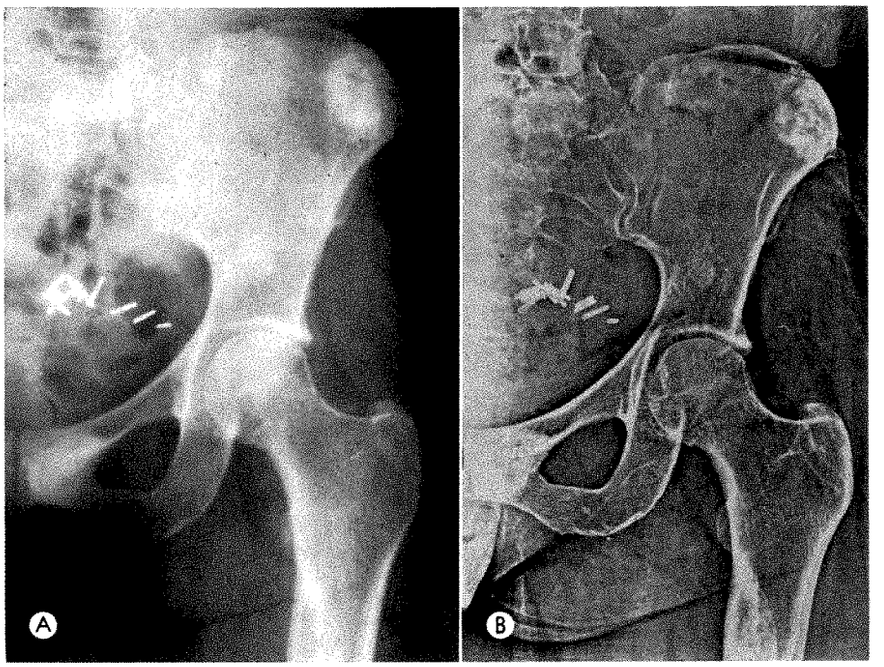


FIG. 5. (*A* and *B*) Metastasis to bones of pelvis from carcinoma of breast. The abnormally dense areas representing the neoplastic disease are usually recorded in good local contrast on the XR (*B*).

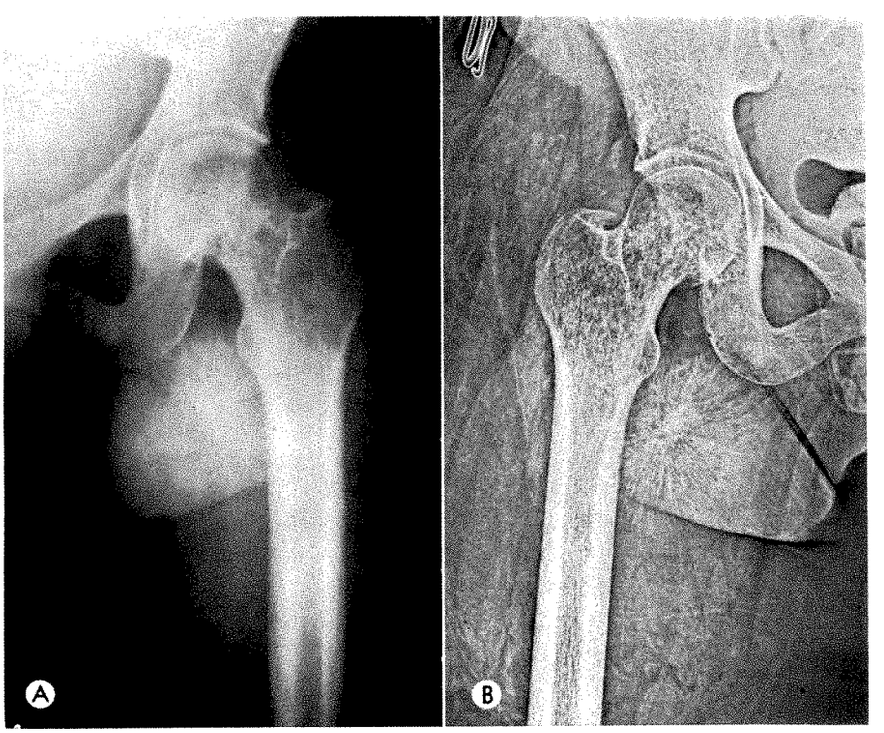


FIG. 6. (*A* and *B*) Extraosseous metastasis of osteogenic sarcoma (lymph node). This 25 year old woman had an amputation of the distal two-thirds of the femur 6 months before. Note the metastatic lesion, soft tissue planes and plastic snap on the perineum in addition to the good visualization of the femur exhibiting changes of atrophy from disuse (*B*).

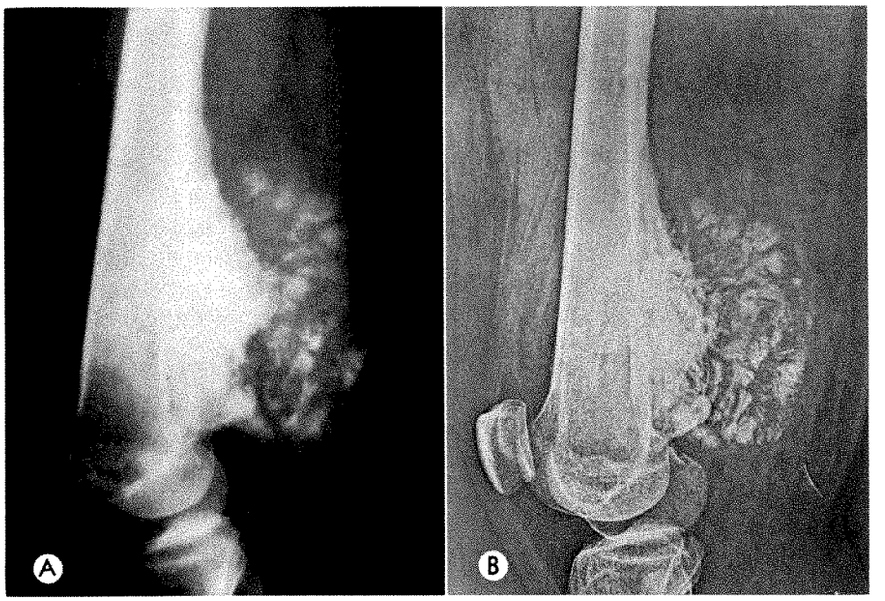


Fig. 7. (*A* and *B*) Osteogenic sarcoma. The large sarcoma is evident on both modes. The XR may have more information in the deeper structures which cannot be seen quite as well even on multiple conventional roentgenographic film images.

structures (Fig. 6, *A* and *B*; and 7, *A* and *B*).

DISCUSSION

The object of the paper is to call attention to the differences that exist between the xeroradiographic and comparable roentgenographic image.

It is important to realize that abrupt differences in density are more likely to be discerned on an XR as opposed to the roentgenogram. Density gradients across the abnormality are greater for xeroradiography and are presented differently due to edge enhancement.

On the other hand, broad area differences in object density are recorded with greater contrast gradients on the roentgenographic film system. They are present but often in lesser contrast on the XR.

Routinely a greater exposure latitude is observed with the XR process. This is advantageous in furnishing readable images of the soft tissues in addition to the underlying osseous structures, but also in occasionally seeing variations in density within an abnormally dense lesion.

CONCLUSION

The image content of the negative xeroradiograph and comparable roentgenographic film image is very similar, but due to inherent physical differences in the 2 systems (photoelectric *vs.* photochemical) is presented in significantly different form and degrees of contrast.

Xeroradiography has a greater x-ray contrast acceptance capability than the roentgenographic film, when considering sharp and abrupt differences in object density, for example, fractures. Roentgenographic film has greater contrast gradients when broad areas, subtle or gradually changing differences in density are concerned.

Xeroradiography has significantly greater recording latitude than its roentgenographic film counterpart.

SUMMARY

Xeroradiography is an electrostatic imaging system based on the photoconductor selenium.

This article discusses contrast and recording latitude of the xeroradiographic

image (XR) and compares it to those of silver halide roentgenographic films.

The study leads one to conclude that both recording systems with proper radiographic exposure factors record similar information, but present it to the interpreter in differing forms as to degrees of contrast and latitude.

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PERCUTANEOUS TRANSBRACHIAL ARTERY INFUSION CATHETER TECHNIQUES*

By GEORGE W. WIRTANEN, M.D.†
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PERCUTANEOUS transbrachial artery techniques for angiographic evaluation of the aorta were described by Boijsen and Feinstein in 1961.[2]

This site has not become as popular as the transfemoral artery approach for diagnostic studies of the branches of the abdominal aorta, but in the treatment of tumors of the upper extremities and tumors supplied by vessels below the diaphragm with chemotherapeutic agents, this approach offers 2 distinct advantages: (1) greater vessel selectivity may be achieved routinely, with more probability that the catheter will remain properly positioned in this vessel for prolonged continuous intraarterial infusion; and (2) the patients are fully ambulatory, have no activity restriction, may be treated as outpatients, and may even return to work, while being treated.

CATHETERIZATION TECHNIQUE

Percutaneous puncture of the brachial artery is done at the junction of the proximal two-thirds and the distal third of the distance between the axilla and the antecubital fossa, with a 4 inch, thin wall, 18 gauge needle. A straight wire guide is passed through the needle and with image intensification and television monitoring is passed to the level of the clavicle. The needle is removed, and a preformed, nonradiopaque, polyethylene catheter, either cold or gas sterilized, with an internal diameter of 1.2 mm. and a wall thickness of 0.25 mm. is introduced into the artery. The wire is removed and an 18 gauge Luer stub adapter and one way flow valve are attached to the catheter (Fig. 1). A mixture of meglumine diatrizoate 52 per cent and sodium diatrizoate 8 per cent is injected to determine catheter position, and the catheter is advanced retrograde through the subclavian artery. If the catheter does not pass the left vertebral artery, it is withdrawn to the level of the clavicle and a J-guide wire facilitates passage to the aortic arch, into the descending aorta, and selectively into the desired vessel.

If 2 catheters are required, as for the internal iliac arteries, or if the patient has an accessory or replaced right hepatic artery, the brachial arteries may be utilized bilaterally (Fig. 2). However, with elongation, tortuosity, and dilatation of the thoracic aorta, usually in patients over the age of 60 years, it becomes more difficult to catheterize the descending aorta with the right brachial artery approach. In these instances, percutaneous puncture of the brachial artery on the left is carried out for both catheters, separating the percu-

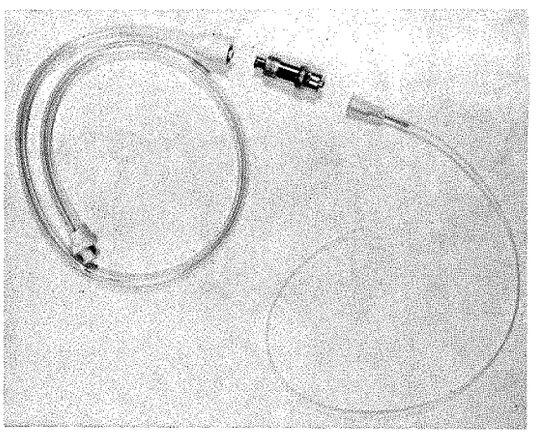


FIG. 1. The indwelling polyethylene catheter is attached to an 18 gauge stub adapter attached to a one way flow valve and then to connecting polyethylene tubing and the infusion bag.

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taneous puncture sites by approximately 2 to 3 cm. This may easily be done, but should infection occur at one of these sites, it will usually involve both sites. Suitable dressings without suture fixation are used, and the catheters are attached to extension tubing and to the infusion bag (Fig. 3). Infusions are usually of 3 weeks' duration for inpatients and 3 months' duration for outpatients.[1] One patient had a 131 day continuous intraarterial infusion. Inpatient catheters and outpatient catheters are checked at regular intervals, usually twice weekly and every other week respectively, fluoroscopically.[6] Catheter displacement, although uncommon, usually requires simple catheter remanipulation. The radial pulse is lost in approximately 20 per cent of the patients, but the distal puncture site allows for sufficient flow through the deep brachial artery, so that thrombectomy has not been necessary in any patient. If patients are to have a repeat infusion, the thrombosis of the artery usually occurs at the percutaneous puncture site, and one may utilize a puncture site 2 to 3 cm. proximally. Individual patients have had as many as 9 courses of infusion, and catheterization has been done on an outpatient basis without hospitalization. Catheterization of the descending aorta has not been possible because of arteriosclerosis in 6 patients, which has necessitated transfemoral artery catheterization of the celiac axis or the hepatic artery selectively, but this approach limits patient ambulation.

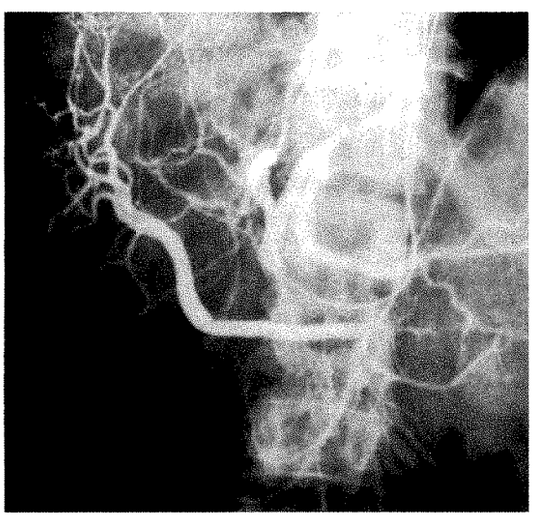


Fig. 2. This 41 year old man had metastatic bronchogenic carcinoma treated in August of 1967 through an indwelling catheter in the replaced right hepatic artery arising from the superior mesenteric artery. This angiogram demonstrates a catheter in the left hepatic artery and a second catheter in the replaced right hepatic, with the earlier infusion having accounted for a reduction in size of the involved right lobe of more than 50 per cent. There is early opacification of the gallbladder wall and contrast material reflux proximally into the other branches of the superior mesenteric artery.

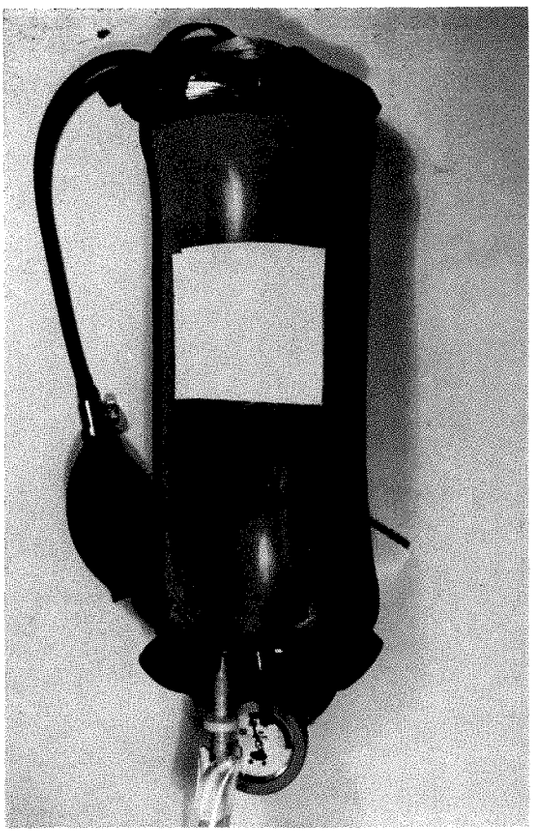


Fig. 3. This commercially available pressure infusor bag is maintained at a pressure of 300 mm. Hg with an inner transfer pack containing a 2 day supply of drug in 1,000 cc. of 5% D/W for inpatients, or a daily drug supply in 150 cc. of D/W for outpatients.

ANGIOGRAPHIC TECHNIQUE

Angiography is altered from the usual

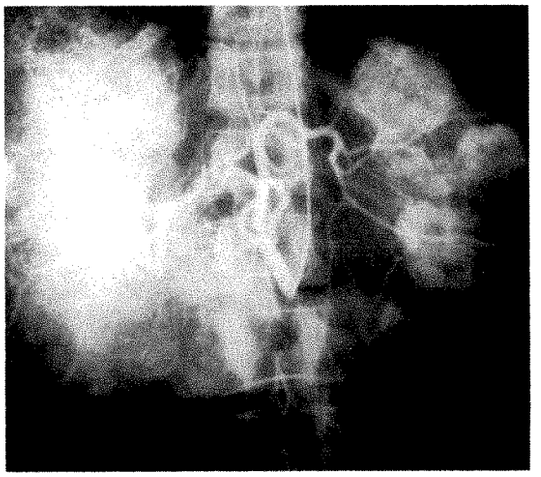


Fig. 4. Selective injection of contrast material into the left hepatic artery demonstrates collateralization to opacify the distal segment of the replaced right hepatic artery which had thrombosed proximally near its origin from the superior mesenteric artery. There is extensive neovascularity in these metastases from adenocarcinoma of the rectum.

diagnostic examination. The small catheter diameter limits flow rates, and consequently quantities of contrast material up to 50 cc. of a mixture of meglumine diatrizoate 66 per cent and sodium diatrizoate 10 per cent are injected into the hepatic, splenic, and superior mesenteric arteries. Injection pressures are altered so that the delivery rate of contrast material is 5 cc./second, irrespective of the volume delivered and this rate does not produce catheter recoil.

Most primary and secondary carcinomas of the liver are hypervascular when compared with noninvolved liver parenchyma (Fig. 4). Contrast material is selectively delivered to areas of neovascularity, and 50 cc. of contrast material so delivered over a time interval of 10 seconds, with portal vein blood flow clearing contrast material simultaneously from normal liver parenchyma, results in enhanced tumor staining.[7] In addition to the arteriographic demonstration of the lesion, serial films of the venous drainage are obtained, and the hepatic veins are frequently visualized. Reverse blood flow with opacification of the hepatic artery and subsequent opacification of the portal vein has been demonstrated in 6 patients. Films are exposed every 2 seconds for 20 seconds and every 5 seconds for 10 seconds.

Angiography of the splenic and superior mesenteric arteries is useful in determining portal vein normalcy and in demonstrating portal hypertension. Examination of these 2 venous structures is also useful in evaluating pancreatic carcinoma; distortion of either vessel gives indirect evidence of pancreatic tumor which may then be correlated with pancreatic tumor angiograms. Fifty cc. of contrast material is utilized in the examination of each of these vessels, injected in 10 seconds, and films are exposed every 3 seconds for 30 seconds (Fig. 5).

Renal,[5] adrenal, gastric, and retroperitoneal tumors may also be evaluated with this approach. Catheterization of the posterior trunk of the internal iliac artery is relatively easy, and if a large anterior trunk is present, it can occasionally be catheterized selectively. Selective catheterization of the deep femoral and the superficial femoral artery is easily accomplished, and one may catheterize to the

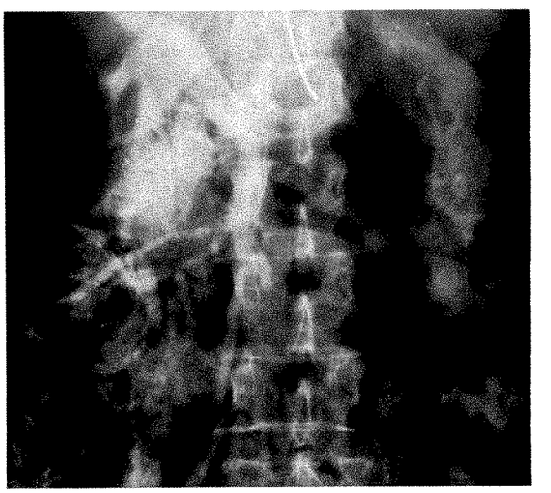


Fig. 5. This superior mesenteric portogram was done by injecting 50 cc. of contrast material into the superior mesenteric artery over a period of 10 seconds, filming at 1 film every 3 seconds over a total elapsed time of 30 seconds.

level of the popliteal artery (Fig. 6).

Angiography is usually done at the time of catheter placement. However, if the contrast medium has produced sufficient patient opacification to render the films technically rather unsatisfactory, angiography may be delayed, with the catheter in place and the infusate running, until the following day. Serial angiograms of the tumor blood supply may thereafter be obtained, as indicated, to the conclusion of therapy. Pharmacologic tumor enhancement,[3] and I^{131} macroaggregated albumin introduced intraarterially[4] may occasionally give additional information regarding liver metastases.

COMPLICATIONS

Infection at the percutaneous puncture site occurs in less than 5 per cent of patients. Two patients early in our experience were treated with systemic antibiotics and their catheters were left indwelling. Both subsequently required surgical intervention, one requiring arterial segmental replacement, with a dacron prosthesis, and the other requiring brachial artery ligation. Five patients have had peripheral septic embolization, secondary to infection at the percutaneous puncture site.



FIG. 6. Percutaneous right brachial artery catheterization of the right superficial femoral artery demonstrates marked neovascularity in this osteosarcoma of the head of the fibula. A minimum tumor dose of 7,000 rads with concomitant continuous intraarterial actinomycin D infusion resulted in only residual osteoid without evidence of tumor cells at the time of above the knee amputation 2 months after completion of therapy.

Subsequent infections have been treated by catheter removal and systemic antibiotic therapy, and no further, similar, complications have occurred.

Following catheter removal because of infection, the opposite brachial artery may be catheterized on the same day, or the homolateral vessel may be recatheterized in 48–72 hours. Two patients who required in excess of 300 cc. of contrast material for catheter placement had immediate post procedure seizures, controlled with barbiturates, without neurologic residue, presumably on the basis of dehydration and contrast medium toxicity. These 2 episodes also occurred early in our experience, and we have subsequently initiated intravenous fluid therapy during the procedure, when these contrast material quantities are approached.

Two patients developed visual field difficulties, one during the catheterization procedure, and the other at the time of catheter removal, both presumably from left vertebral artery embolization of either an arterial plaque or an external catheter thrombus.

One patient with a replaced right hepatic artery arising from the superior mesenteric artery, which proved to be an exceptionally difficult vessel in which to maintain catheter position, had repeated catheter remanipulations with subsequent superior mesenteric artery thrombosis, surgical intervention, and postsurgical death.

Approximately 2–3 per cent of patients have hepatic artery occlusion, but this has not resulted in patient mortality. It does, however, eliminate the hepatic artery as a route of administration of drug, and occasionally subsequent infusion is possible through collateral arteries, such as the inferior pancreatico-duodenal, the inferior

diaphragmatic arteries, and 1 patient has had 3 courses of infusion via the left gastric artery which filled the common hepatic artery by way of the right gastric artery, without any associated gastric toxicity.

SUMMARY

Over 1,000 percutaneous transbrachial artery catheterizations have been performed for the placement of nonradiopaque polyethylene catheters for intraarterial chemotherapeutic infusions since 1965.

Catheters have been left indwelling up to 131 days for continuous infusion.

Thrombectomy has not been required in any patient, and catheter superselectivity was achieved with full patient ambulation without activity restriction.

Large volume, slow injection rate angiography (infusion angiography) provides quality film studies of arterial and venous structures.

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A SIMPLIFIED AND RELIABLE CANNULATION TECHNIQUE FOR LYMPHOGRAPHY*

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SINCE the original technique for lymphography by cannulation of lower limb lymphatics was described by Kinmonth[4] in 1955, many papers[2,3,5,6] on improved techniques have been published.

There are 2 main drawbacks to most of the techniques thus far described: (a) these techniques stress securing the lymphatic vessel to the needle by means of a clamp or ligature which requires additional manipulation of the lymphatic vessel after cannulation; and (b) these methods require specialized equipment, albeit often simple and inexpensive, which frequently must be constructed, if it is not commercially available.

TECHNIQUE

1. A preliminary roentgenogram of the abdomen is obtained and evaluated. If residual contrast material from previous lymphography is noted in the lymph nodes, additional roentgenograms in multiple projections are obtained to be used subsequently in evaluation of the lymph nodes opacified in the current study.

2. The patient is placed supine on the examination table and the feet are prepared and draped. If available, a fluoroscopic table is preferable as progress of the contrast material can be rapidly monitored; however, a routine roentgenographic table or a nonroentgenographic situation with a portable roentgen-ray unit may be used. One half milliliter of an equal mixture of 4 per cent direct sky blue dye* and 1 per cent Lidocaine hydrochloride is injected intradermally into the dorsum of the first and second interdigital web spaces of each foot.

3. Approximately 15 to 30 minutes later, a local anesthetic agent is injected into the skin of the dorsum of each foot at the base of the 1st and 2nd metatarsals, and an incision 2 to 3 cm. long is made. The initial incision is carefully made through the dermis and subsequent exposure obtained by blunt dissection. The lymphatic channel, which is now visible due to the blue dye, is isolated and dissected free of adherent tissues to preclude the possibility of extravascular injection.

4. Two silk ligatures approximately 20 cm. in length are then placed under the lymphatic vessel. To proximally occlude and distend the lymph vessel, the first ligature is then retracted superiorly and taped to the skin. Distention of the lymphatic vessel may be increased by massaging the dorsum of the distal aspect of the foot. We prefer use of a Band Aid which has had the backing material removed from half of the adhesive surface. This permits use of taping material which has excellent adhesive material on the exposed end but the covered end does not stick to the surgical gloves.

The second ligature is then retracted inferiorly, drawn through the first or second interdigital space and a small hemostat clamped onto the ends. This traction is then maintained by the weight of the hemostat.

The superior and inferior retraction lifts the lymphatic vessel from the site of the incision, fixes its position and makes it readily accessible for subsequent cannulation (Fig. 1).

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The views expressed in this paper are those of the author and do not necessarily reflect the views of the United States Army or the Department of Defense.

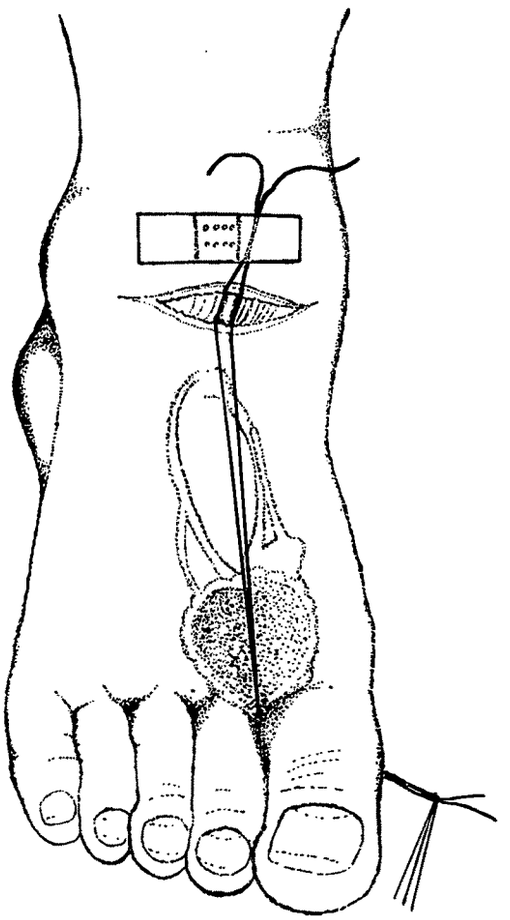


FIG. 1. The isolated lymphatic vessel is immobilized, occluded and distended by the upper ligature and further immobilized by the lower ligature.

5. We use a commercially prepared disposable lymphographic set† consisting of a needle attached to a 60 cm. length of polyethylene tubing. We select a 27 or 30 gauge needle, depending on the size of the lymphatic vessel. The lymphatic vessel may be further immobilized by applying additional manual traction on the lower ligature. The tubing which is attached to the needle is then drawn between the digits (the same interdigital space through which the lower ligature was drawn previously) and the needle is placed with the tip several mm. into the lymphatic channel. The needle during cannulation may be held with an appropriate instrument or hand held; however, we prefer hand holding the needle as the subsequent release is more smoothly accomplished.

The Band Aid on the upper ligature is then gently removed which releases the proximal occlusion of the lymphatic vessel. No ties or clamps are placed around the lymph channel or the needle. Not tying the vessel to the needle at this point greatly reduces the manipulation of the vessel and is very important, since it is at this point with other methods that we have seen most failures. Another advantage with not tying or clamping the vessel to the needle is that if the injection is made too rapidly, leakage distal to the injection site may occur, but the vessel does not rupture proximally.

The base of the needle is then taped to the skin, again using another Band Aid or a piece of tape (Fig. 2).

6. The injection device is then connected and injection of ethiodized oil accomplished over a 1 to 2 hour period depending on the size of the cannulated lymphatics.

We use the Harvard pump;‡ however, a simple gravity device described by Dolan and Moore[1] may be used which would eliminate the need for this expensive piece of equipment. Contrast material is injected until bilateral opacification of the upper lumbar lymphatics is seen. The maximum amount of contrast material used is 10 ml. per side in the adult patient.

7. Following injection, the needle is carefully removed and the ligatures withdrawn. No vessels must be tied and no foreign material is left in the incision. The skin is closed.

The limbs are then exercised with the patient recumbent to allow any residual contrast material in the lymphatics of the limbs to pass upward. This also allows the patient to move and relax prior to roentgenography.

8. Follow-up anteroposterior, lateral and oblique roentgenograms of the pelvis and

† Cook Incorporated, 925 South Curry Pike, Bloomington, Illinois 47401.

‡ Harvard Apparatus Co. Inc., Dover, Massachusetts.

abdomen as well as anteroposterior roentgenograms of the chest are obtained at the end of injection and 24 hours later. Excretory urography may be performed during the 24 hour roentgenograms if desired.

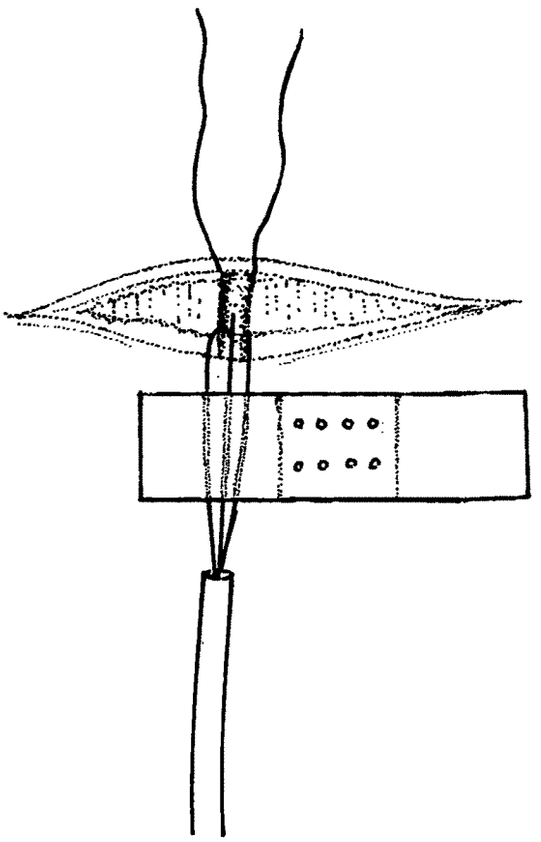


FIG. 2. Following cannulation the needle is taped in place. The lymphatic vessel remains untied which has greatly decreased the amount of necessary manipulation after cannulation.

SUMMARY

A simplified and reliable technique for lymphography is presented.

This differs significantly from previous descriptions in that lymphatic manipulation is greatly decreased by not tying or clamping the lymphatic vessel to the needle after cannulation.

No special equipment is required.

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BIOLOGICAL PROPERTIES OF ^{252}Cf*

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THE availability of ^{252}Cf provides an opportunity to utilize a unique modality, protracted high LET irradiation, in the treatment of malignant growths. The theoretical gain which may be realized by the interstitial or intracavitary use of californium sources is due to the low oxygen enhancement ratio (OER) of such radiations. This may be significant in the treatment of tumors that may be in part anoxic or hypoxic.

To be balanced against this potential advantage are a number of factors, actual and theoretical, which detract from the application of californium to clinical problems. Aside from the short half-life (2.6 years) and difficulties in providing accurate dosimetry there are biological problems and interrelated physical problems that complicate the utilization of these sources. These include the factors of mixed radiations with varying ratios at depth, problems of shielding, a complicated relationship of relative biological effect (RBE) to dose rate, and radiological health hazards. In addition, the acquisition of background radiobiological data is hampered by difficulties in performing biological experiments at low dose rates.

At this time considerable information has become available on biological aspects of californium irradiation. This information includes studies at a chromosomal level, on cells and on intact tissues. Careful consideration of this information is required as a preliminary to clinical application.

DOSIMETRY

Detailed aspects of dosimetry have been treated elsewhere.[8,19–21] This aspect is mentioned only briefly here to indicate that practical problems exist in clinical dosimetry. The decay of sources requires a continuous correction in dosage calculations. This can be a source of confusion with regard to maintaining an inventory of sources unless careful consideration is undertaken of when and how replacement of sources is to be carried out. The variation of neutron to gamma ratio with distance from sources affects the RBE. The RBE value may differ considerably from point to point within an irradiated volume. It may also be affected by the variation in dose rate within this volume.

RELATIVE BIOLOGICAL EFFECT (RBE)

The RBE of californium has been studied in relation to effects in cells and tissues. The problem in these studies is to evaluate the effect of dose rate on the value for the RBE. Also, the fraction of total absorbed dose delivered by ^{252}Cf neutrons is a function of source encapsulation, distance from source, and extent of surrounding hydrogenous material. Therefore, in order to obtain meaningful comparisons, RBE values should be measured for the neutron component alone. A crude first approximation would be to assume that the gamma component has a negligible effect. A more accurate evaluation would relate the slope of mixed radiation survival curves to the slope of survival curves for neutron and gamma components alone:

$$\frac{1}{D_0(n+\gamma)} = \frac{F_n}{D_0(n)} + \frac{F_\gamma}{D_0(\gamma)},$$

where F_n and F_γ represent the fraction of total absorbed dose delivered by neutrons and gamma rays respectively.[14] In general, $D_0(\gamma)$ will not be known. If it is assumed

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TABLE I

RBE OF ^{252}Cf

Biological system (and reference)		^{252}Cf total dose rate (rads/hr.)	n/γ for ^{252}Cf radiations	γ Dose rate of ^{137}Cs or ^{226}Ra standard	RBE (total dose)	RBE (neutrons only)
HeLa Cells (10)*	37°C	16.0	1.7	31	2.89	3.95
HeLa Cells (1, 2)	30°C	20	1.95	60	2.15	2.74
HeLa Cells (this paper)	37°C	~13	1.7	37.3		4.38
Hamster Cells (18)	37°C	1.27–5.21	1.23–1.59	11.7–52.5	10–5	16–7.7
Hamster Cells (14)	22°C	1.14–21.6	1.23–1.59	11.7–52.5	4.3 (^{226}Ra = 35.3 rads/hr.)	6.7
Hamster Cells (this paper)	37°C	~13.5	1.33–1.7	37.3		3.94
Vicia Faba (17)		16.02	1.32	46.9	6.5–5.3	10
Mouse Jejunal Crypt Cells (25)		43.5	1.55	160	3.2	5
Pig Skin (3)		12–53	1.7	35–192		7.4–5.4
		11.1		50		6.6
Mouse Spleen Colony (7)		10.81	1.32	42.9	1.81	2.44

* No. in parentheses indicates reference number.

that $D_0(\gamma)$ equals D_0 for the electromagnetic radiation relative to which the RBE is being calculated, the equation for RBE reduces to

$$RBE = \frac{D_{em} - D_\gamma}{D_n}.$$

Here, D_{em}, and $D_n + D_\gamma$ are doses from standard electromagnetic radiation, and the mixed ^{252}Cf field, respectively, which produce the same end point in the same irradiation time.

Table 1 presents the RBE data available to date. Where necessary, the data have been manipulated to produce the RBE for neutrons alone, as outlined above. Results from single cell survival curves published so far indicate (either by direct measurement or extrapolation) an RBE of from 2.7 to 4.4, relative to the clinically interesting dose rate of 30–50 rads/hour for the standard gamma radiation.[1,2,10,18] An exception to this is the RBE of 6.7 obtained by Hall,[14] who circumvented the effects of cell division during irradiation by carrying out the irradiations at room temperature.

Evaluation of radiation effects on tissues have in general given higher RBEs. Withers *et al.*[25] found an RBE of 5 for mouse jejunal crypt cells, which they extrapolated to approximately 7 for ^{226}Ra at 35 rads/hour. Atkins *et al.*[3] reported an RBE of 6.6 for pig skin, relative to ^{137}Cs at 50 rads/hour.

Effects on the hemopoietic system have been studied by Carsten.[7] In a study on spleen colony-forming ability the RBE for californium neutrons was 2.44 compared to gamma irradiation. Dose rates were 10.81 rads/hour (n+γ) from ^{252}Cf and 42.9 rads/hour from ^{182}Ta. This is consistent with a somewhat lower RBE for hemopoietic tissues compared to other tissues for neutrons as shown by Field.[13]

Recently, experiments with Chinese hamster cells have been completed at this laboratory in order to measure RBE and OER for ^{252}Cf. Survival curves were obtained at 37°C, so that during irradiation, cells progressed through the cell cycle. Therefore, changing cellular multiplication as shown in Figure 1 complicates any evaluation. Survival curves for various dose rates of ^{252}Cf and ^{137}Cs are presented in Figure 2. D_0's, obtained with ^{137}Cs at 16 rads/hour and 37.3 rads/hour were 1,500 and 500 rads, respectively, while an acute irradiation with 250 kvp x rays yielded a D_0 of 140 rads. An RBE was obtained relative to the ^{137}Cs at 37.3 rads/hour, by evaluating the $D_0(n)$ of ^{252}Cf (from a plot of $D_0(n)$ *vs.* irradiation time) which produced a 10 per cent survival in the same time as

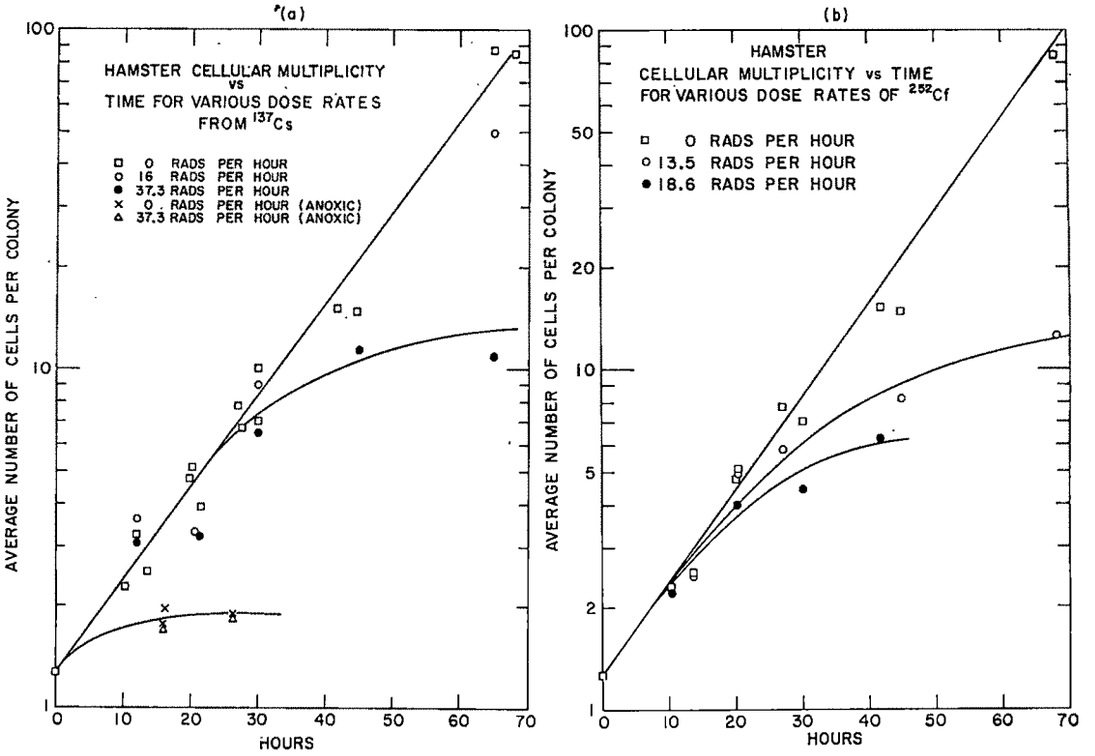


FIG. 1. Effect of various dose rates of ^{137}Cs, and ^{252}Cf on Chinese hamster cell multiplicity.

that needed for ^{137}Cs (34.2 hours). The D_0's from the ^{252}Cf survival curves in Figure 2 are shown in Table II, along with n/γ ratios, and times to reach 10 per cent survival. The RBE thus obtained was 500/127 = 3.94.

Similarly, an RBE can be obtained for HeLa cells, if the ^{252}Cf $D_0(n+\gamma)$'s which we have measured over the course of 5 years are used to obtain a $D_0(n)$ which produces a 1 per cent survival in the same time that was needed for ^{137}Cs at 37.3 rads/hour (32.7 hours; D_0 = 230 rads).[9] Table III lists the D_0's, ^{252}Cf dose rates, and time needed to achieve 1 per cent survival. A plot of $D_0(n)$ *vs.* irradiation time for 1 per cent survival allowed an RBE evaluation of 230/52.5 = 4.38. This value should be inherently more accurate than the RBE of 3.95 which we obtained previously with 2 single survival curves,[10] but is within 11 per cent of the latter measurement.

It is not immediately clear why most of the RBEs measured to date with single cell survival curves are significantly smaller than those evaluated with tissues.

OXYGEN ENHANCEMENT RATIO (OER)

Determinations of the oxygen enhancement ratio with californium 252 have been consistent with other determinations performed with various sources of fast neutrons. Since OER is not a sensitive function of the ^{252}Cf gamma component, reports

TABLE II

^{252}Cf total dose rate (rads/hr.)	n/γ	$D_0(n+\gamma)$	$D_0(n)$*	Duration of irradiation 10% survival (hours)
13.5	1.33	215	130.4	35.9
18.6	1.33	155	92.4	19.6
27.0	1.70	110	71.2	10.0

* Assuming a D_0 of 1,500 rads for the γ components of 6 to 10 rads/hr.

have in general been made on the basis of total dose (n+γ). Measurements with californium 252 have been made using growth of *Vicia faba* seedlings,[17] chromosome aberrations in Chinese hamster cells[6] and survival of P-388 leukemia cells,[5] HeLa cells,[1,2,9] and hamster cells.[15] OER measurements (Table IV) show quite good agreement, with values generally ranging from 1.4 to 1.75. The value of 2.0[5] was obtained at a dose rate of 200–260 rads per hour. At these very high dose rates, the gamma component becomes increasingly effective, thus increasing the OER. It is unlikely that ^{252}Cf would be used at such dose rates.

Our recently completed Chinese hamster cell experiments (Fig. 3) produced an OER of 1.7 for ^{252}Cf at 27 rads/hour which is in agreement with the above ($D_{0's}$ = 110 and 190 rads for oxygenated and anoxic survival curves, respectively). Techniques used in the hamster cell experiments are the same as those reported by Drew *et al.*,[9] and Fairchild *et al.*[12] The survival of control cells in these experiments is of prime importance, since unless certain precautions are taken, prolonged anoxia will prove toxic. The survival of unirradiated control cells *vs.* duration of anoxia is shown in Figure 4, both for the recent hamster cell studies and for HeLa cells.[9] A survival of approximately 80 per cent is demonstrated for periods of anoxia lasting up to 40 hours.

There has been some indication that irradiation with gamma rays at low dose rates gives a very low OER, comparable to that obtained with californium.[24] We have been able to demonstrate an OER of 2.50 for gamma irradiation at 37.3 rads/hour with HeLa cells[9] and 2.5 (50 per cent survival) for a dose rate of 37.3 rads/hour

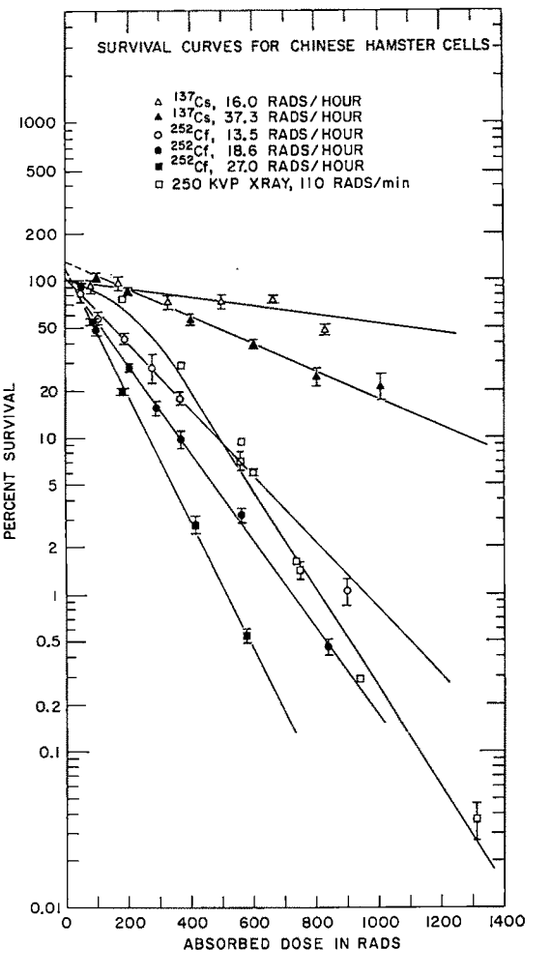


FIG. 2. Effect on Chinese hamster cell survival of irradiation by ^{137}Cs, ^{252}Cf, and 250 kvp x rays.

TABLE III

^{252}Cf total dose rate (rads/hr.)	n/γ	$D_0(n+\gamma)$	$D_0(n)$*	Duration of irradiation, 1% survival (hours)	Ref.
6.15	1.7	123	90.3	96.7	11
9.09	1.7	85	59.4	47.9	11
16.0	1.7	72	49.5	24.0	11
19.4	1.7	61	41.3	17.5	9

* Assuming a D_0 of 320 rads/hr. for the γ component of 2.3 to 7.2 rads/hr.[16]

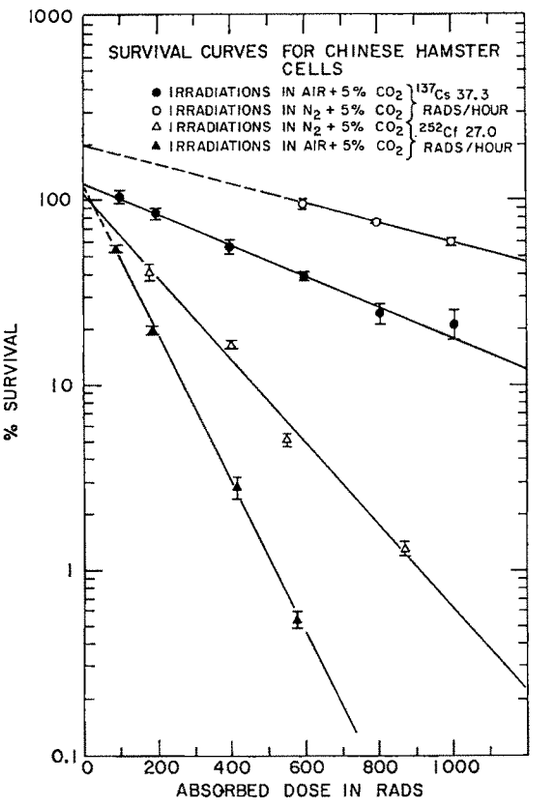


FIG. 3. Chinese hamster cell survival under oxygenated and anoxic conditions after irradiation by ^{137}Cs and ^{252}Cf.

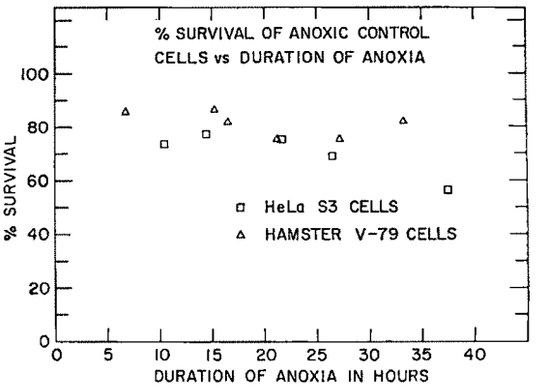


FIG. 4. Effect of anoxia on survival of HeLa cells and Chinese hamster cells.

with Chinese hamster cells (Fig. 3). These values are in agreement with other data becoming available,[1,2,5] and are not significantly different from OERs observed with acute x-ray irradiation. This increases the significance of the low OER values found with californium.

HAZARDS

Biological considerations suggest caution in the use of californium 252 in a hospital environment. The lack of recovery from cellular damage due to neutrons results in high values for relative biological effectiveness, particularly for low doses and low dose rates. This situation exists outside the treatment volume in interstitial implants with californium. Therefore it is not a simple matter to extrapolate from the experience with radium and other gamma sources insofar as effects on non-tumor tissue is concerned.

TABLE IV

OER OF ^{252}Cf

Biological System (and reference)		^{252}Cf total dose rate (rads/hr.)	Cf OER	γ (^{137}Cs or ^{226}Ra) dose rate (rads/hr.)	γ OER	Acute x-ray exposure OER
Vicia Faba (17)*		16.02	1.66	46.9	2.02	2.7
Hamster Cell chromosome aberration frequency (6)		60.4	1.75			
P-338 Leukemia Cells (5)	(37°C)	200–260	2.0	300–420	2.6	
HeLa Cells (9)	(37°C)	19.4	1.55	37.3	2.5	3.0
HeLa Cells (1, 2)	(30°C)	20	1.7	60	2.53	2.85
Hamster Cells (15)	(22°C)	16.5	1.4			
Hamster Cells (this paper)	(37°C)	27.0	1.7	37.3	2.5	

* No. in parentheses indicates reference number.

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EDITORIALS

MORE ON THE *r* AND *c* UNITS AND SOME OTHER RELATED UNITS

IN March 1965, exactly 8 years ago, an Editorial[1] in this JOURNAL dealt in great detail with the fascinating history of the dosage of radiation and the specifications arrived at for prescribing it in medical application. Since that time, great progress has been made not only in the domain of radiation therapy, but also in the field of several of the allied sciences, so that it appears appropriate to re-analyze the present status of these specifications and to determine whether any new, even more far reaching, suggestions have been, or are being, made.

The r unit. After laborious investigations of several methods such as chemical, photographic, fluorescent, and biologic, extending over more than 2 decades, the ionization method was chosen as the most accurate and most practical for specification of dosage. At the Second International Congress of Radiology in Stockholm,[2] in 1928, the following recommendations of the International X-Ray Unit Committee were accepted: (1) that an international unit of x-radiation be adopted; (2) that this international unit be the quantity of x-radiation which, when the secondary electrons are fully utilized and the wall effect of the chamber is avoided, produces in 1 cc. of atmospheric air at 0° C. and 76 cm. mercury pressure such a degree of conductivity that 1 esu of charge is measured at saturation current; and (3) that the international unit of x-radiation be called "The Röntgen," and that it be designated by the letter small *r*.

The measurement of the *r* in standardized form constituted an enormous task. The arduous enthusiasm and the many outstanding contributions of Taylor and his associates of the National Bureau of Standards, Washington, D. C., were of inestimable aid, so that at the Third International Congress of Radiology in Paris, in 1931, Taylor[3] was able to present the final report on "The international comparison of x-ray standards." The condenser type of dosimeter devised by Glasser and Seitz[4] in 1928, and known subsequently as the Victoreen condenser *r* meter, has become, and still is, the most widely used clinical instrument for measuring the radiation in medical application.

The *r* unit was then extended to include radium and at the Fifth International Congress of Radiology in Chicago, in 1937, it was redefined as follows:[5] The roentgen shall be the quantity of x- or gamma-radiation such that the associated corpuscular emission per 0.001293 gram of air (the mass of 1 cc. of dry atmospheric air at 0°C. and 760 mm. mercury pressure) produces, in air, ions carrying 1 esu of quantity of electricity of either sign.

At the Sixth International Congress of Radiology in London, in 1950, the *r* continued to be recognized, its definition unchanged, as the unit of x- and gamma-ray quantity of "dose."[6] However, to correlate the dose of any ionizing radiation with its biologic or related effect, the recommendation was made that the dose be expressed in terms of the quantity of energy absorbed per unit mass (ergs per gram) of irradiated material at the place of interest. This led to the unit rad (roentgen absorbed dose) which was provisionally accepted at the Seventh International Congress of Radiology in Copenhagen, in 1953,[7] and formally adopted in 1956. It was defined as the unit of "absorbed dose" of any ionizing radia-

tion, equal to 100 ergs per gram of any absorber. The unit of the quantity of radiation delivered to a certain place was still called the roentgen (designated by the symbol small *r*), but to distinguish it from the absorbed dose was named the "exposure dose," and later simply "exposure."

The specified use of the *r* and rad was followed by introduction of several "dose equivalent" units, such as: the rem (roentgen equivalent man); the rep (roentgen equivalent physical); and more recently the ret (roentgen equivalent therapeutic). Of these, the rem, which is the unit of RBE (relative biologic effect), is the most important, since it is utilized both in radiobiology and radiation protection, although lately efforts are being made to devise another, more meaningful, unit for radiation protection.

In 1962,[8] at the recommendation of an *Ad Hoc* Committee, "several recognized international groups working in the field of symbols and nomenclature including the International Council of Scientific Unions have agreed upon the convention that the first letter of abbreviations of units named after individuals should be capitalized," and it was decided to apply this also to the *r* unit. Based on this convention, *r*, rad, rem, rep, and more recently ret should be written as R, Rad, Rem, Rep, and Ret. Yet, more than a decade later, we find that with the sole exception of R, the roentgen in all other abbreviations is not capitalized.

The c unit. The curie unit has an even more fascinating history. After the early experience with emanation, Turner,[9] in 1909, proposed the milligram hour (mg.-hr.) as the unit for specification of the dosage of radium and in 1910 the curie was adopted as the unit of measurement for the emanation (mcδ=millicurie destroyed). One mc, or 1/1000th curie, was defined as the quantity of emanation in equilibrium with 1 mg. of radium element.

Pursuant to recommendations made at the Fourth International Congress of Radiology in Zürich, in 1934, at the Fifth International Congress, held in Chicago in 1937, it was adopted—as already stated—that the *r* also be accepted as the international unit for measurement of the quantity of the gamma rays. Then, at the Seventh International Congress of Radiology, in Copenhagen, in 1953, it was adopted that the gamma-ray emission should be expressed in terms of r/mc-hr. at 1 cm. from a point source. The curie was officially chosen as the unit of radioactivity and was defined as the quantity of any radioactive nuclide in which the number of disintegrations per second is 3.7×10^{10}. Its symbol, as that of its counterpart, was written with the "small letter" *c*.

In 1962,[8] in line with the recommendations of the *Ad Hoc* Committee, it was decided to also capitalize the *c*. However, since this involved confusion with other capitalized C symbols (as for example C for Coulomb or C. for Centigrade), the symbol Ci was devised and such commonly used abbreviations as mc-hr., r/mc-hr., μc/gm., were replaced with mCi-hr., R/mCi-hr., μCi/g., etc.

At this time, a second change was made in relocating the various exponents identifying the symbol of a radioactive element. Originally, the most commonly used exponent for identification of the radioactive element, which is the atomic weight, was placed as superscript on the right side of the symbol. This might have been due to the psychologic impact of the common knowledge facts: that the overwhelming population of the human race is right-handed; that the traffic in the majority of countries moves on the right side; that all the mathematical exponents (10^{10}, 96° F., 6′, 10″ etc.) are superscripts on the right side; and that all the chemical valencies (H_2O, H_2SO_4, etc.) are subscripts on the right side.

Whatever the reason, the formula was:

$$_{Z}\text{Symbol}^{M},$$

where M is the mass or atomic weight of the element and Z is the atomic number. Since Z has little usage in identification of the radioactive element, it was hardly ever

utilized, and the simplified writing of the symbol was I^{131}, $Tc^{99m}O_4$ etc.

This formula was changed by placing the most commonly used exponent as superscript on the left side of the symbol, and locating the others as follows:

$$^{M}_{Z}\,\text{Symbol}\,^{E}_{M_o},$$

where M is the mass, Z is the atomic number, E indicates the electric charge when in an ionized state, and M_o refers to the molecular or valency state.

As in the original formula, the exponents less important for specification were rarely used and the simplified formulas of ^{131}I, $^{99m}TcO_4$, etc., emerged. In other words, whatever is used is placed now as a superscript on the left side, instead of on the right side of the symbol. For example, with the exception of very few instances, we find radioactive elements specified as ^{99m}Tc, ^{113m}In, ^{87m}Sr, whereas according to the above formula should be $^{99}Tc^{m}$, $^{113}In^{m}$ and $^{87}Sr^{m}$ and there are not infrequently other nonconformities in location of some of the other exponents.

USAN nomenclature of radioactive pharmaceuticals. Because of the continuously increasing use of radioactive pharmaceuticals in the diagnosis and treatment of disease, and in many fundamental research investigations, the United States Adopted Names (USAN) Council in 1963 undertook to adopt nonproprietary names for radioactive pharmaceuticals and made a study of the existing styles of nomenclature. The results were published in 1966 in the *Journal of the American Medical Association*.[10,11] The fundamental principle was adopted that for these drugs the nonproprietary designation should include the name of the basic compound serving as the carrier for the radioactivity, the symbol for the radioactive isotope, and the atomic weight (since several radioactive isotopes of a given element may be in use). A cumulative table of the nonproprietary names of the radioactive pharmaceuticals available at that time was included.

The style of the nomenclature is illustrated by the following 2 examples:

(1) Isotope ^{131}I: nonproprietary name, diotyrosine I 131 (supplied as Diotyrosine I 131); ethiodized oil I 131 (supplied as Ethiodol I 131); and some 18 other I 131 labeled drugs;

(2) Isotope ^{99m}Tc: nonproprietary name, sodium pertechnetate Tc 99m (supplied as Sodium Pertechnetate Tc 99m); technetium Tc 99m (supplied as TechneKow Tc 99m; Technetope, Tc 99m-Sulfide Colloid).

The USAN Council emphasized that the selected style is notable for its clarity, simplicity, and the ease with which it lends itself to typewriting and typesetting, there being no parentheses, hyphens, superscripts or brackets.

The SI system and metrication. The SI system (Système International d'Unités) is an extension of the old cgs (centimeter, gram, second) absolute system. It is founded on seven basic units: the meter (m), unit of length; kilo-gram (kg), unit of mass; second (s), unit of time; degree Kelvin (°K), unit of temperature; ampère (A), unit of electric current; candela (cd), unit of light intensity; and the mole (mol), unit of molecular quantity. Its purpose is international metrication within the feasible future.

As regards measurement of the ionizing radiations is concerned, the units involved are the R, Ci and rad and even more contentiously the rem. In a correspondence to the *British Journal of Radiology*,[12] W. A. Jennings, secretary of the British Committee on Radiation Units and Measurements writes "In Germany and Belgium the special units of Ci, R, and rad may be used in accordance with the ICRU definition until December 31, 1977, after which they cease to be recognized for legislative purposes in both countries, unless, in the case of Belgium, an extension is formally granted." In October 1971, The Council of the European Economic Committee (EEC) also ratified a directive on units and measurements, which provides for exclusive use by January 1, 1978 of a prescribed system of

metric units, strongly based on the SI system. The strict application of this system could eventually lead to abandonment of the roentgen, curie and rad, as measuring units of the ionizing radiation.

In ICRU Report 19,[13] issued July 1, 1971, the 3 basic units of measurement of ionizing radiation are defined as follows:

$$1 \text{ roentgen} = 2.58 \times 10^{-4} \text{ Ckg}^{-1} \text{ (exactly)}$$
$$1 \text{ curie} = 3.7 \times 10^{10} \text{ s}^{-1} \text{ (exactly)}$$
$$1 \text{ rad} = 10^{-2} \text{ Jkg}^{-1}$$

In other words, Ckg^{-1} (1 Coulomb per kilogram) would be the symbol of the derived SI unit of 1 roentgen; s^{-1} (reciprocal second) the symbol of the derived SI unit of 1 curie; and Jkg^{-1} (1 Joule per kilogram) the symbol of the derived SI unit of 1 rad.

The ICRU in its Report 19 "considers that the establishment of additional special units in the field of dosimetry is undesirable, but continues to recognize the existing special units."

The Editors of the *British Journal of Radiology*[14] also have reservations about the practicability of introducing such complicated physical units for the clinical application of radiation therapy, and on the eve of the Thirteenth International Congress of Radiology to be held in October 1973 in Madrid, they ask the ICRU to take the lead in considering the various problems involved, and present some recommendations for solution of this extremely complex facet of the medical aspect of radiology.

As regards the usage of nomenclature and symbols, the ICRU, in 1956, recommended that every country modify them according to its own practices. Thus, one may write kev, keV, or Kev; ^{14}C or C^{14}; rad per unit time, rad per time, or rad divided by time; rad/sec, rad/s, or $\text{rad} \cdot \text{s}^{-1}$.

As stated in the former Editorial,[1] the American Journal of Roentgenology, Radiation Therapy & Nuclear Medicine followed, and still follows, a style which is based on 2 important principles: In articles dealing with subjects of the allied fields such as pure physics, radiobiology, physical chemistry, pharmacology and particularly radioactive pharmaceuticals, the nomenclature and symbols are used as developed in each respective field.

"In the domain of medical radiology, as a result of a practice initiated in 1912, and consistently followed since then, a style has been built which has become a characteristic feature of the Journal."

In attempting to unravel the tangle of the various units and the many accepted or proposed alterations since the discovery of x rays in 1895 and of radium in 1898, one is reminded of Oersted's famous experiment of 1820. Hans Christian Oersted, a Danish physicist, in discovering the link between electricity and magnetism, found that when a compass needle was placed *below* the conductor of an electric current the North end of the compass was deflected to the *left* (the observer facing the South). He assumed that the electric current was flowing from the North pole (+) to the South pole (−). When the compass was placed *above* the electric conductor, the opposite occurred. The positive pole or electrode eventually was called "anode," and the negative pole or electrode was called "cathode." Today, more than one and a half century later, we still call the "anode" an anode and the "cathode" a cathode, but we know that the electron emission in an x-ray tube emanates from the cathode and not from the anode.

The SI system, in metricating, may be weighted with similar situations.

Traian Leucutia, M.D.

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FRANK A. RIEBEL, M.D.
1903-1972

DR. FRANK A. RIEBEL died June 7, 1972, in Mercy Hospital, Columbus, Ohio, where he was Chairman of the Department of Radiology. He died from a cerebral infarct, which occurred while he was working in his department.

He was born in Columbus, Ohio, October 29, 1903. He attended the Columbus Public Schools and completed his premedical work at Ohio State University in 1923. He received his M.D. from the Ohio State University in 1925 and did graduate work at the University of Vienna in 1925. He served his internship at the Metropolitan Hospital in New York City in 1927, and then took his residency in Radiology at Montefiore Hospital, also in New York City, in 1928.

Frank was the son of the late Dr. John

Augustus and Mabel Riebel. His father was a prominent Columbus surgeon and his mother was an attorney. Frank is survived by his wife, Violet Riebel; two sons, Michael S. Riebel and Frank A. Riebel; three daughters, Dr. Barbara Griffith, Mrs. David (Nancy) Snow, and Miss Linda K. Riebel; and seven grandchildren.

After Frank completed his radiology residency he returned to Columbus where he practiced radiology and general medicine, with his father, for a number of years. Finally, in 1951, he limited his practice to radiology when he became the radiologist at Mercy Hospital, a position he held until his death. During his last years he saw his plans and dreams reach fruition with completion of the new Mercy Hospital facility, including a fine, contemporary Department of Radiology.

Frank was a remarkable man. He was warm, energetic, creative, generous, and had a tremendous hunger for knowledge. He was something of a prodigy, having graduated from medical school at age twenty-two, and having passed the Ohio Bar examination the same year. He never attended law school formally, but read law as a pastime while in medical school. Later he passed the Federal Bar.

While in school, he was a Big Ten fencing champion and alternate on the Olympic fencing team. From 1929 to 1942 Frank coached the Ohio State University fencing team and retired after his team won the National Collegiate Athletic Association Championship in 1942. Frank was Chairman of the NCAA fencing committee from 1944 to 1948, and also a member of the Olympic Committee in 1948.

Frank remained vigorous and energetic also in his later years, even following a serious heart attack. Elevators were an anathema to him; he bounded up steps two at a time. Walking with Frank was a struggle just to keep up. He did not set a leisurely pace.

A keen student of foreign languages, Frank had a passing knowledge of at least 8 different languages. For many years he abstracted foreign language radiologic literature for the AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE and for *Radiology*. A number of years ago, Frank submitted a scientific paper to a Russian medical journal which was returned unpublished two years later. His paper did, however, prompt an editorial in the journal on the "misguided" American radiologist.

Frank was a member of many local, state, and national societies, including the American Medical Association, the Central Ohio Radiological Society, the Ohio State Radiological Society, and the Radiological Society of North America. He was a Fellow in the American College of Radiology and was formerly president of the Central Ohio Radiological Society. As a result of his scientific achievements he had been invited to become a member of the American Roentgen Ray Society, but passed away 3 months before final action was to be taken.

Frank was also an Associate Clinical Professor of Radiology at The Ohio State University College of Medicine, where he was active for many years in the teaching of residents and medical students. He was one of the most loyal and productive members of the faculty and his regular attendance at departmental functions set an outstanding example for everyone. He spent every Wednesday afternoon in the department with the residents who found in him a superb and dedicated teacher, a friendly colleague and an astute clinical radiologist. His calm philosophical approach to difficult situations and his great concern for the individual sick patient endeared him to faculty and students alike.

He was a member of the Masonic Blue Lodge, Scottish Rite, and Shrine. He was for many years an active member of the First Community Church in Columbus.

Frank Riebel was a warm, wise, stimulating, and interesting man. He had a great desire to learn and know. He was a fine physician. He was young and creative his entire life. His death is a deep loss for his family, friends and colleagues.

STEWART P. CHASE, M.D.
SIDNEY W. NELSON, M.D.

NEWS ITEMS

ELECTRONIC IMAGING TECHNIQUES IN DIAGNOSTIC RADIOLOGY

This course is sponsored by the Department of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania, and will be held April 13–14, 1973. It is designed to acquaint radiologists with the basic principles of electronic imaging and storage techniques, and their most recent application to various clinical problems.

Subjects to be covered include: the fundamentals of video and digital image recording systems; magnetic disk and storage tube techniques; and recent developments in the generation of high resolution computer calculated tomograms. Clinical experience to be described includes: applications to neuroradiology, neurosurgery, angiography, cardiology, gastrointestinal fluoroscopy, and spot filming as well as dose reduction in pediatrics and obstetrics.

Presentations will consist of Lectures and Panel Discussions by an outstanding Guest Faculty as well as members of the staff of the Department of Radiology.

For further information please contact: E. Ralph Heinz, M.D., Department of Radiology, University of Pittsburgh School of Medicine, Presbyterian-University Hospital, Pittsburgh, Pennsylvania 15213.

POSTGRADUATE COURSE IN CARDIOVASCULAR RADIOLOGY

This postgraduate course in cardiovascular radiology is organized by the Department of Radiology of the Albert Einstein College of Medicine and its affiliated hospitals and will be held May 14–18, 1973. The course is intended for radiologists and other physicians interested in heart disease. Attention will be directed toward the practical aspects of specialized diagnostic procedures. A comprehensive review of current concepts of pathology and physiology as well as radiology of the cardiovascular system will also be presented. A "Case of the Day" discussion by a distinguished radiologist will emphasize the approach to diagnostic problems.

The Program Chairmen are: Milton Elkin, M.D., Professor and Chairman, Department of Radiology, Albert Einstein College of Medicine, and Harold G. Jacobson, M.D., Professor and Chairman, Department of Radiology, Albert Einstein College of Medicine (Montefiore Hospital and Medical Center).

The Program Committee consists of Michael K. Kauff, M.D., Stephen W. Schoenbaum, M.D., and Melvin N. Zelefsky, M.D.

The distinguished Guest Faculty includes: Drs. Herbert L. Abrams, Harold A. Baltaxe, Murray Baron, M. Paul Capp, Erik Carlsson, Simon Dack, Jesse E. Edwards, Larry P. Elliott, Kent Ellis, Florencio A. Hipona, Melvin P. Judkins, Richard G. Lester, Abraham M. Rudolph, Mason Sones, Israel Steinberg, Manuel Viamonte, Jr., and Fred Winsberg, in addition to the Local Faculty.

For further information and application for registration please write to Milton Elkin, M.D., Program Chairman Cardiovascular Radiology Postgraduate Course, Albert Einstein College of Medicine, Bronx, New York 10461.

REFRESHER COURSE IN RADIOBIOLOGY —THE PHYSICS OF RADIOLOGY AND NUCLEAR MEDICINE

A short refresher course in radiobiology and the physics of radiology and nuclear medicine will be presented at Queens Hospital Center, on 3 consecutive afternoons, May 21–23, 1973.

This course is directed primarily towards 2nd and 3rd year radiology residents who are preparing for their board examinations in radiology.

The faculty includes: Harry Astarita, Chief Physicist, Nassau Hospital; Edwin Holodney, Chief Physicist, St. Vincents Medical Center; Lillian Jacobson, Chief Physicist, Long Island Jewish Hospital;

Donald Pizzarello, Radiobiologist, New York University Medical College; and Gerald Shapiro, Chief Physicist, Queens Hospital Center.

Further information and application forms can be obtained from: Jan J. Smulewicz, M.D., Director, Department of Radiology, Queens Hospital Center, 82-68 164th Street, Jamaica, New York 11432.

SYMPOSIUM ON RADIOIMMUNOASSAY AND RELATED PROCEDURES IN CLINICAL MEDICINE AND RESEARCH

The above symposium is arranged by the International Atomic Energy Agency (IAEA), in Istanbul, Turkey, September 10–14, 1973.

The program of this Symposium, the second to be organized by the International Atomic Energy Agency in the subject field, will cover all aspects of radioimmunoassay and related procedures and their applications. Particular attention will be given to the *in vitro* determination of substances of clinical interest such as hormones, vitamins and drugs. Sections of the program will be devoted to recently developed techniques for the detection of tumor, viral and bacterial antigens, and to assays employing labelled antibodies and naturally occurring specific receptors.

Further information, participation forms and forms for submission of a paper intended for presentation at the Symposium will be obtainable from national authorities for atomic energy matters. Abstracts of such papers must be submitted to the International Atomic Energy Agency through these authorities.

The Scientific Secretaries are: Dr. E. J. Garcia and Dr. E. H. Belcher, Medical Applications Section, IAEA, Kärntner Ring 11–13, A-1010 Vienna, Austria.

X SYMPOSIUM NEURORADIOLOGICUM

The X Symposium Neuroradiologicum will be held in Punta del Este, Uruguay, on March 10–16, 1974.

Contributions dealing with all branches of neuroradiology, including pararadiologic examinations and radiation therapy, will be accepted.

The following main topics have been chosen: 1. The spine and the spinal cord; 2. Advances in encephalography and ventriculography; 3. Influence of intracranial and intraspinal hypertension on circulation, especially the venous phase; 4. Diagnosis of posterior fossa lesions; 5. Advances in cerebral blood flow examinations and collateral circulation.

Scientific and industrial exhibitions will be arranged.

Charter flights from Europe and the United States will be organized as required; to facilitate the arrangements, early applications will be appreciated.

For further information please apply to: President, Dr. Néstor Azambuja or Secretary General, Dr. Andrés de Tenyi; for Industrial exhibition to Mr. Gabriel Benquet.

The address is Hospital de Clinicas, Piso 2, Montevideo, Uruguay.

ABDOMINAL RADIOLOGY

The Department of Continuing Education of Harvard Medical School announces a course in Abdominal Radiology to be held under the direction of Richard C. Pfister, M.D. and Joseph T. Ferrucci, Jr., M.D. of the Department of Radiology, Massachusetts General Hospital, April 2–6, 1973.

This is an intensive five day course designed to present a review of current concepts of the radiology of abdominal disorders. Major emphasis will be directed to the gastrointestinal and genitourinary systems. The program is organized into two days each of gastrointestinal and genitourinary diagnostic radiology separated by a day of general abdominal topics of significant current interest.

The faculty will consist of distinguished guests and members of the Massachusetts General Hospital and other Harvard Medical institutions.

For further information please write to: Associate Dean, Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, Massachusetts 02115.

BOOK REVIEW

Acute Cholecystitis. By Clarence J. Schein, M.D., Professor of Surgery, Albert Einstein College of Medicine of Yeshiva University and Montefiore Hospital Medical Center, Bronx, N. Y. Cloth. Pp. 324, with 179 illustrations. Price, $17.50. Harper & Row, 49 East 33rd Street, New York, N. Y. 10016, 1971.

In this impressive book, the author has integrated his large personal experience with a careful review of the literature for a comprehensive and balanced discussion of acute cholecystitis and its complications.

An introductory chapter of historical background and biographic sketches acknowledges the contributions of the great surgeons of the nineteenth and early twentieth century.

Acute cholecystitis affects 20 to 25 per cent of patients with symptomatic cholelithiasis. While it may be simplified as resulting from obstruction in association with an altered intravesical milieu, there is a detailed discussion of the investigative and clinical evidence of the multiple etiologic factors. Another section provides an excellent correlation of the pathophysiology of the disease with clinical data. Other chapters on clinical diagnosis, medical management, operative technique, and operative and postoperative problems and complications reflect a consistently practical approach sharpened by evident experience.

The chapter on roentgen diagnosis is notable for its inclusiveness and clarity. It underscores the recognition that the proper management of acute cholecystitis requires accurate radiologic interpretation. The indications, value and pitfalls of plain film roentgenography, intravenous cholangiography, oral cholecystography, selective arteriography, and operative and postoperative cholangiography are clearly detailed. The physiologic basis of cholangiographic interpretation and the advantages of cholangiomanometry, often combined with operative cholangiography, are explained. Both of these are based on many of the author's original observations. Minor oversights include the use of the term "decubitus" for a supine roentgenogram of the abdomen, and the illustrated labelling of pressure by a distended gallbladder on the hepatic flexure as "cecum."

A concluding section on special problems deals, among other aspects, with the common bile duct and pancreatic problems in acute cholecystitis, acalculus cholecystitis, acute cholecystitis following cholecystoenterostomy, emphysematous cholecystitis, and the postcholecystectomy syndrome.

The book is designed primarily for the surgeon involved in the acute abdomen and particularly the biliary system. It does recognize that improvements in the care of patients with acute cholecystitis have accompanied advances in roentgenology that allow for preoperative confirmation of the diagnosis and for the intraoperative evaluation of the extrahepatic biliary tree. Furthermore, it provides a comprehensive understanding of the pathogenesis of acute cholecystitis in a variety of situations, its complications and their radiologic evaluation. For these reasons, it would be a valuable addition to a radiologist's library.

Morton A. Meyers, M.D.

BOOKS RECEIVED

A Text-Book of X-Ray Diagnosis. By British Authors. Volume II. Fourth edition. Edited by S. Cochrane Shanks, C.B.E., M.D., F.R.C.P., F.F.R., Consulting Radiologist, University College Hospital, London; and Sir Peter Kerley, K.C.V.O., C.B.E., M.D., F.R.C.P., F.F.R., D.M.R.E., Consulting Radiologist, Westminster Hospital and National Heart Hospital, London, England. Cloth. Pp. 671, with 581 illustrations. Price, $28.00. W. B. Saunders Company, West Washington Square, Philadelphia, Pa. 19105, 1972.

Comprehensive Review for the Radiologic Technologist. Second edition. By Matthew Stevens, R.T., Director, Radiologic Technology, Northeastern University, Boston, Mass.; and Robert I. Phillips, R.T., F.A.S.R.T., Director of Radiologic Services, The Methodist Hospital, Houston, Texas. Cloth. Pp. 229, with 19 illustrations. Price, $8.75. C. V. Mosby Company, 11830 Westline Industrial Drive, St. Louis, Mo. 63141, 1972.

Acute Ureteric Obstruction: A Clinical and Radiological Study. By P. M. Bretland, M.D., D.M.R.D., F.F.R., Lt. Col. R.A.M.C. (Retired), Consultant Radiologist, Whittington Hospital, London; Lecturer, University College Hospital Medical School, London; Formerly, Consultant Radiologist, British Military Hospital, Singapore.

Cloth. Pp. 219, with some illustrations. Price, $18.50. Appleton-Century-Crofts, 440 Park Avenue South, New York, N. Y. 10016, 1972.

Controlled Therapeutic Trials in Cancer. Guidelines and List of Trials. Edited by R. Flamant. UICC Technical Report Series. Volume 8. Paper. Pp. 103. Price, $3.00. International Union Against Cancer, Geneva, 1972.

Angiography of Trauma. By Whei-Rung Fu, M.D., Associate Professor of Radiology, Georgetown University School of Medicine; Consultant in Radiology, Veterans Administration Hospital and St. Elizabeth's Hospital, Washington, D. C.; Formerly, Assistant Professor of Radiology, George Washington University School of Medicine, Washington, D. C. Cloth. Pp. 106, with many illustrations. Price, $11.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62717, 1972.

X-Ray Microscopy in Clinical and Experimental Medicine. By T. A. Hall, Senior Technical Officer, Cavendish Laboratory, University of Cambridge, Cambridge, England; H. O. E. Rockert, Associate Professor of Histology, University of Göteborg, Faculty of Medicine, Göteborg, Sweden; and R. L. deC. H. Saunders, Professor of Anatomy, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, Canada. Cloth. Pp. 320, with some figures. Price, $24.75. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62717, 1972.

Laboratory Manual and Workbook in Radiologic Technology. By Charles A. Jacobi, B.Sc., R.T.(A.R.R.T.), M.T.(A.S.C.P.), Associate Professor and Chairman, Department of Radiologic Technology, College of Allied Health Professions, University of Nevada, Las Vegas, Nevada; Member, Radiological Safety Board, University of Nevada System; Formerly, Assistant Professor and Chairman, Department of Medical Radiologic Technology, and Member, Radioisotopes Committee, Oregon Technical Institute, Klamath Falls, Oregon; and Duane T. Pierce, B.S., M.A., R.T.(A.R.R.T.), Lecturer, Department of Radiologic Technology, College of Allied Health Professions, University of Nevada, Las Vegas, Nevada; Formerly, Chief Technologist and Director, School of Radiologic Technology, St. Francis Hospital, Wichita, Kansas. Paper. Pp. 364, with 304 illustrations. Price, $7.50. C. V. Mosby Company, 11830 Westline Industrial Drive, St. Louis, Mo. 63141, 1972.

Cisternography and Hydrocephalus: A Symposium. Edited by John C. Harbert, M.D., Assistant Professor of Medicine and Radiology; Director, Division of Nuclear Medicine, Georgetown University Hospital, Washington, D. C. With the Assistance of David C. McCullough, M.D., Associate Editor, Instructor in Neurosurgery, Division of Neurosurgery, Georgetown University Hospital; Alfred J. Luessenhop, M.D., Associate Editor, Associate Professor of Surgery; Chief, Division of Neurosurgery, Georgetown University Hospital; and Giovanni Di Chiro, M.D., Associate Editor, Chief, Section on Neuroradiology, National Institute of Neurological Diseases and Stroke, Bethesda, Md.; Clinical Professor of Radiology, Georgetown University Hospital. Cloth. Pp. 559, with many illustrations. Price, $44.50. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill. 62717, 1972.

Que Faire Devant un Cancer? By Bernard Pierquin, Professeur à la Faculté de Médecine de Créteil; Chef du Service de Carcinologie Radiothérapique de l'Hôpital Henri Mondor; and François Baillet, Chef de Clinique à la Faculté de Médecine de Créteil. Paper. Pp. 98, with 15 figures. Price, 15 F. Masson & Cie, 120, Boulevard Saint-Germain, Paris-6e, France, 1972.

Purulent and Fibrous Mediastinitis: Radiological Diagnosis. By St. Z. Leszczyński, M.D., in collaboration, L. Pawlicka, M.D. Cloth. Pp. 158 with many illustrations. Price, $6.00. Polish Medical Publishers, Warsaw, 1972. In U.S.A., United States Department of Commerce, National Technical Information Service, Springfield, Va. 22151. Control No. TT 70-55171.

Aspects of Medical Education in Developing Countries. Selected Papers Presented at the Second WHO Conference on Medical Education in the Eastern Mediterranean Region. World Health Organization, Geneva. Public Health Papers, No. 47. Paper. Pp. 113. Price, $2.00. The American Public Health Association, Inc., 1015 Eighteenth St. N.W., Washington, D. C. 20036, 1972.

Dynamic Aspects of Brain Scanning. Edited by Jyoji Handa, M.D., Department of Neurological Surgery, Faculty of Medicine, Kyoto University, Kyoto, Japan. Cloth. Pp. 250, with 450 illustrations. Price, $22.50. University Park Press, Chamber of Commerce Building, Baltimore, Md. 21202, 1972.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 25–28, 1973.

AMERICAN RADIUM SOCIETY
Secretary, Dr. Felix N. Rutledge, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025. Annual Meeting: Broadmoor Hotel, Colorado Springs, Colorado, April 22–26, 1973.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. Hillier L. Baker, Jr., Mayo Clinic, Rochester, Minn. 55901. Annual Meeting: Palmer House, Chicago, Ill., November 25–30, 1973.

AMERICAN COLLEGE OF RADIOLOGY
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago, Ill. 60606. Annual meeting: San Francisco, Calif., April 2–7, 1973.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. Antolin Raventos, Davis, Calif. Annual Meeting: New York, N. Y., June 24–28, 1973.

AMERICAN BOARD OF RADIOLOGY
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler East, Rochester, Minn. 55901.

Oral examinations will be held in the following cities during the next 2 years: Chicago, Ill., June 4–8, 1973, Marriott Motor Hotel; Dallas, Tex., Dec. 3–7, 1973, Statler Hilton Hotel; New York, N. Y., June 10–14, 1974, New York Hilton Hotel; and Los Angeles, Calif., Dec. 9–13, 1974, International Hotel.

Written examinations are scheduled in 13 large centers on June 16, 1973.

Applications must be received in the Board Office before Sept. 30 of the year preceding the one in which the candidate wishes to be examined.

Deadline for filing applications for any examination in 1974 is September 30, 1973.

AMERICAN BOARD OF NUCLEAR MEDICINE, INC. A Conjoint Board of the American Boards of Internal Medicine, Pathology and Radiology and sponsored by the Society of Nuclear Medicine.
Chairman, Dr. Merrill A. Bender, Suite 2402, 211 E. 43rd St., New York, N. Y. 10017.

Examination for certification in the Specialty of Nuclear Medicine will be given April 7, 1973. The deadline for filing application forms was January 1, 1973.

AMERICAN ASSOCIATION OF PHYSICISTS IN MEDICINE
Secretary, D. John Wright, Ph.D., Department of Radiology, Temple Univ. Health Sciences Center, Philadelphia, Pa. 19140. Annual Meeting in San Diego, Calif., July 29–Aug. 3, 1973.

AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGISTS
Secretary, Dr. Herman D. Suit, Radiation Medicine, Massachusetts General Hospital, Boston, Mass. 02114. Annual Meeting.

AMERICAN INSTITUTE OF ULTRASOUND IN MEDICINE
Secretary, John M. Reid, Ph.D., 556 18th Ave., Seattle, Wash. 98122. Annual Meeting.

AMERICAN SOCIETY OF NEURORADIOLOGY
Secretary, Dr. David O. Davis, Department of Radiology, 901 Twenty-third St., N. W., Washington, D. C. 20037. Annual Meeting, Boston, Mass., April 26–28, 1973.

THIRTEENTH INTERNATIONAL CONGRESS OF RADIOLOGY
President-Elect, Dr. Juan Gómez López. *Secretary General*, Dr. José Bonmatí, Lagasca, 27 Madrid 1, España. Meeting: Madrid, Spain, Oct. 15–20, 1973.

INTERNATIONAL SOCIETY OF RADIOLOGY
Hon. Secretary-Treasurer, Prof. Eric Samuel, Radiologist-in-Charge, The Royal Infirmary, Edinburgh EH3 9Y-W, Scotland.

ELEVENTH INTER-AMERICAN CONGRESS OF RADIOLOGY
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colorado 80907. Meeting: Bogotá, Colombia in 1975.

INTER-AMERICAN COLLEGE OF RADIOLOGY
President, Dr. Miguel Dao y Dao, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A.
Secretary General, Dr. Rubén Merenfeld, Instituto Diagnóstico, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A. Meeting: Bogotá, Colombia in 1975.

THIRD CONGRESS OF THE EUROPEAN ASSOCIATION OF RADIOLOGY
Meeting in June, 1975 in Edinburgh, Scotland.

SECOND ASIAN AND OCEANIAN CONGRESS OF RADIOLOGY
Honorary Secretary, Dr. J. J. Martin, Box 805 F., G.P.O., Melbourne, 3001, Australia.
Meeting in 1975.

ALABAMA CHAPTER OF ACR
Secretary-Treasurer, Dr. Lowry R. Young, Jr., 905 Madison St., Huntsville, Ala. 35801. Meets time and place of Alabama State Medical Association.

ALASKA RADIOLOGICAL SOCIETY
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

AMERICAN THERMOGRAPHIC SOCIETY
Secretary-Treasurer, Dr. Marc. S. Lapayowker, Department of Radiology, Temple Univ. Hosp., 3401 N. St., Philadelphia, Pa. 19140. Meets at New York-Hilton Hotel, June 23 and 24, 1973.

ARIZONA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Wesley S. Fee, 2421 E. 6th St., Tucson, Ariz. 85719. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

ARK-LA-TEX RADIOLOGICAL SOCIETY
Secretary, Dr. Erich K. Lang, Confederate Memorial Medical Center, LSU School of Medicine, Shreveport, La. 71101.

ARKANSAS CHAPTER OF ACR
Secretary-Treasurer, Dr. David H. Newbern, 4301 W. Markham, Little Rock, Ark. 72205. Meets twice annually, the Spring Meeting being in conjunction with and at the place of the State Medical Association.

ASSOCIATION OF UNIVERSITY RADIOLOGISTS
Secretary-Treasurer, Dr. Melvyn H. Schreiber, 2909 Dominique Dr., Galveston, Tex. Annual Meeting, Vancouver, B. C., Canada, May 9–12, 1973.

ATLANTA RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Ernst Ruder, Dept. of Radiol., Crawford Long Memorial Hosp., Atlanta, Ga. 30308. Meets on four Thursday evenings during the academic year at a time announced in early September of each year, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

BAVARIAN-AMERICAN RADIOLOGIC SOCIETY
Secretary, Lucien F. Burke, Maj. MC, Radiol. Service, US Army Gen. Hosp., Frankfurt, APO, New York 09757.

BLOCKLEY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

BLUEGRASS RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Eugene Slusher, Lexington

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Clinic, 1221 S. Broadway, Lexington, Ky. 40504. The Society meets once each month during the school year.

BRONX RADIOLOGICAL SOCIETY, NEW YORK STATE, CHAPTER ACR
Secretary-Treasurer, Dr. Leon J. Corbin, 1369 Rosedale Ave., Bronx, N. Y. 10472. Meets 4 times a year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Sarah Lieberson, 1298 St. Marks Ave., Brooklyn, N. Y. 11213. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Ru-Kan Lin, 191 North St., Buffalo, N. Y. 14201. Meets second Monday evening each month, October to May inclusive, at University Club.

CALIFORNIA RADIATION THERAPY ASSOCIATION
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets semiannually in San Francisco and Los Angeles.

CALIFORNIA RADIOLOGICAL SOCIETY, CALIFORNIA CHAPTER OF ACR
Secretary-Treasurer, Dr. John L. Gwinn, 4650 Sunset Blvd., Los Angeles, Calif. 90027.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P.O. Box 10, Rutherford College, N. C. 28671. Meets every Thursday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:30 P.M.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. John Sanborn, Radiology Department, Crouse-Irving Memorial Hosp., Irving Ave., Syracuse, N. Y. 13210. Meets first Monday each month October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Terry Meyer, 175 S. Merkle Rd., Columbus, Ohio 43209. Meets second Thursday in October, November, January, and March 15, and May 19 at Fort Hayes Hotel, Columbus, Ohio.

CHICAGO RADIOLOGICAL SOCIETY, DIVISION OF THE ILLINOIS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Raymond L. Del Fava, 355 Ridge Ave., Evanston, Ill. 60202. Meets third Thursday of each month, October to April, except December, at the Bismarck Hotel, Chicago, Ill.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Alvin Segel, 3395 Scranton Rd., Cleveland, Ohio 44109. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

COLORADO RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Jerome D. Sutherland, 3705 E. Colfax Ave., Denver, Colo. 80206. Meets third Friday of each month at Denver Athletic Club from September through May.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meets in April and October.

DALLAS-FORT WORTH RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Lee Radford, 6011 Harry Hines, Suite 900, Dallas, Tex. 75235. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Tex.

DELAWARE CHAPTER OF ACR
Secretary, Dr. Seymour R. Kaplan, Kent Gen. Hosp., Dover, Del. 19901.

EAST BAY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Peter E. Kane, Children's Hosp. Med. Ctr., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

EAST TENNESSEE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George H. Wood, 205 Medical Arts Bldg., Knoxville, Tenn. 37902. Meets in January and September.

FLORIDA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Ralph C. Aye, Tampa General Hospital, Tampa, Fla. 33606. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. J. C. Hewitt, 1 Davis Blvd., Tampa, Fla. 33606. Meets in January, March, May, July, September and November.

GEORGIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Richard S. Colvin, Emory University Clinic, Atlanta, Ga. 30322. Meets in spring and fall at Annual State Society Meeting.

GREATER CINCINNATI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

GREATER LOUISVILLE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

GREATER MIAMI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Stanley I. Worton, 1400 N.W. 10th Avenue, Miami, Florida 33136. Meets monthly, third Wednesday at 8:00 P.M. at various member hospitals, Miami, Fla.

GREATER ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary-Treasurer, John J. Lang, 507 Fairways Circle, St. Louis, Mo. 63141.

HAWAII RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Raymond W. Brust, Jr., St. Francis Hosp., 2260 Liliha St., Honolulu, Hawaii 96817. Meets third Monday of each month at 7:30 P.M.

HEALTH PHYSICS SOCIETY
Secretary, Shirley D. Vickers, Catholic Medical Center of Brooklyn and Queens, 88-25 153rd St., Jamaica, N. Y. 11432. Annual Meeting: Deauville Hotel, Miami Beach, Fla., June 17–21, 1973.

HOUSTON RADIOLOGICAL SOCIETY
Secretary, Dr. Neill B Longley, 6436 Fannin, Suite 601, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

IDAHO STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Hugh P. Smith, Jr., 130 E. Bannock, Boise, Id. 83702. Meets in the spring and fall.

ILLINOIS RADIOLOGICAL SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. B. Jay Hill, Mercy Hospital, Stevenson at King Drive, Chicago, Ill. 60616. Meets in the spring and fall.

INDIANA ROENTGEN SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. L. Ray Stewart, 852 S. Alvord Blvd., Evansville, Ind. 47714.

IOWA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. John Huston Jr., 1948 First Ave. N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ralph H. Baehr, 310 Medical Arts Bldg., Topeka, Kan. 66604. Meets in spring with State Medical Society and in winter on call.

KENTUCKY CHAPTER OF ACR
Secretary-Treasurer, Dr. Joseph G. Whelan, Jr., 1313 St. Antony Place, Louisville, Ky. 40204. Meets in April and September.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N.Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

KNOXVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Jerome Zwanger, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. Gabriel H. Wilson, UCLA Center for Medical Sciences, Los Angeles, Calif. 90024. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif. Midwinter Radiological Conference.

Louisiana Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Robert T. Cook, Southern Baptist Hosp., 2700 Napoleon Ave., New Orleans, La. 70115.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Tex. 77701.

Maine Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Richard W. Taylor, Radiology Department, St. Mary's General Hospital, Lewiston, Maine 04240. Meets in June, September, December and April.

Maryland Radiological Society, Chapter of ACR
Secretary, Dr. George Burke, 4000 North Charles St., Baltimore, Md. 21218.

Massachusetts Radiological Society, Chapter of ACR
Secretary, Dr. Norman L. Sadowsky, The Faulkner Hosp., 1153 Centre St., Jamaica Plain, Mass. 02130.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Jerry C. Phillips, The University of Tennessee College of Medicine, Department of Radiology, Walter C. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday Oct. through May at the University Club.

Miami Valley Radiological Society
Secretary, Dr. Darwood B. Hance, Reid Memorial Hospital, Richmond, Ind. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Michigan Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. George A. Kling, Harper Hospital, 3825 Brush St., Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. Thomas C. Lipscomb, 1004 North Tenth St., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Harlan W. Hawkinson, 6 Buffalo Rd., St. Paul, Minn. 55110. Meets twice annually, fall and winter.

Mississippi State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Nancy W. Burrow, 1327 Peachtree St., Jackson, Miss. 39202. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ronald G. Evens, Mallinckrodt Institute of Radiology, 510 S. Kingshighway, St. Louis, Mo. 63110.

Montana Radiological Society, Chapter of ACR
Secretary, Dr. Dexter W. Johnson, Columbus Hosp., Great Falls, Mont. 59401.

Nebraska Chapter of ACR
Secretary-Treasurer, Dr. John T. McGreer, III, 924 Sharp Bldg., Lincoln, Nebr. 68508. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society, Chapter of ACR
Secretary, Dr. William G. Arbonies, 887 Marsh, Reno, Nev. 89520.

New England Roentgen Ray Society
Secretary, Dr. Stefan C. Schatzki, 1180 Beacon St. Brookline Mass. 02146. Meets the third Friday of each month, October through April, excluding December, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

New Hampshire Roentgen Ray Society, Chapter of ACR
Secretary-Treasurer, Dr. Edward P. Kane, Claremont Gen. Hosp., Claremont, N. H. 03743. Meets four to six times yearly.

New Mexico Society of Radiologists, Chapter of ACR
Secretary, Dr. Carole R. Simmons, Dept. of Radiol., Presbyterian Hospital Center, Albuquerque, N. M. 87106. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New Orleans Radiological Society, Inc.
Secretary-Treasurer, Dr. Jimmy L. Mains, P.O. Box 446, Gretna, La. 70053. Meets bimonthly at local restaurants selected by the President.

New York Roentgen Society
Secretary-Treasurer, Dr. Howard R. Gould, 153 West 11th Street, New York, N. Y. 10011. Meets monthly on the 3rd Monday at the New York Academy of Medicine at 4:30 P.M. Annual Spring Conference, Waldorf-Astoria Hotel, New York, N. Y., Apr. 26–28, 1973. Further information may be obtained from Dr. Albert A. Dunn, Roosevelt Hosp., New York, N. Y. 10019.

New York State Chapter of ACR
Secretary-Treasurer, Dr. John J. Magovern, 74 N. Village Ave., Rockville Centre, N. Y. 11570.

North Carolina Chapter of ACR
Secretary-Treasurer, Dr. Ernest B. Spangler, Wesley Long Hosp., Greensboro, N. C., 27402. Meets twice a year. The Spring Meeting is held at the time of the meeting of the North Carolina Medical Society. The Fall Meeting is held in November at the Mid Pines Club, Southern Pines, N. C.

North Dakota Radiological Society, Chapter of ACR
Secretary, Dr. Marshall Landa, 1702 13th St., So., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. David F. Bew, University Hospital of Jacksonville, 655 W. Eighth Street, P.O. Box 2751, Jacksonville, Florida 32203. Meets quarterly in March, June, September and December.

Northeastern Oklahoma Radiological Society
Secretary-Treasurer, Dr. Theodore J. Brickner, Jr., 5919 S. Gary Place, Tulsa, Okla. 74110.

Northeastern New York Radiological Society
Secretary, Dr. Robert C. Friedman, 325 Presidential Way, Guilderland, N. Y. 12085. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiation Therapy Association
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets quarterly.

Northern California Radiological Society
Secretary, Dr. J. Richard McProuty, 6620 Coyle Ave., Carmichael, Calif. 95608. Meets fourth Monday of Nov., Jan., and March at the Mansion Inn, Sacramento, Calif.

Northwestern New York Radiological Society
Secretary, Dr. Barbara E. Chick, Glens Falls Hospital, Glens Falls, N. Y. 12801.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society, Chapter of ACR
Secretary, Dr. Thomas F. Ulrich, Barberton Citizens Hospital, Barberton, Ohio 44203.

Oklahoma State Radiological Society, Chapter of ACR
Secretary, Dr. George H. Ladd, 4616 Denison, Muskogee, Okla. 74401. Meets in January, May and October.

ORANGE COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Norman Arnett, 400 North Pomona, Fullerton, Calif. 92632. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

OREGON STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ronald W. Philips, 2305 Washington, Milwaukie, Ore. 97222. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Oregon 97005. Annual meeting: Benson Hotel, Portland, Ore., May 11–13, 1973.

PENNSYLVANIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Theodore A. Tristan, Harrisburg Polyclinic Hosp., Harrisburg, Pa. 17105.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Howard M. Pollack, Department of Radiology, Episcopal Hospital, Philadelphia, Pa. 19125. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Stephen C. Bruno, Shadyside Hospital, 5230 Centre Ave., Pittsburgh, Pa. 15232. Meets second Wednesday of month, September through May, at the Pittsburgh Athletic Association.

RADIATION RESEARCH SOCIETY
Executive Secretary, Richard J. Burk, Jr., 4211 39th St., N.W., Washington, D. C. 20016. Annual Meeting: St. Louis, Mo., April 29–May 3, 1973. International Congress of Radiation Research, Seattle, Wash., July 14–20, 1974.

RADIOLOGICAL SOCIETY OF CONNECTICUT, INC., CHAPTER OF ACR
Secretary-Treasurer, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meetings are held quarterly.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary-Treasurer, Dr. Alvin Nathan, c/o Academy of Medicine, 320 Broadway, Cincinnati, Ohio 45202. Meets first Monday of each month at Cincinnati Academy of Medicine.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
President-Secretary, Dr. Arch W. Templeton, Univ. of Kansas Med. Ctr., Kansas City, Kansas 66103. Meets 5 times a year on given dates.

RADIOLOGICAL SOCIETY OF LOUISIANA, CHAPTER OF ACR
Secretary-Treasurer, Dr. Robert T. Cook, 1820 Octavia St., New Orleans, La. 70115. Meets semiannually during Louisiana State Medical Society meeting and 6 months later.

RADIOLOGICAL SOCIETY OF NEW JERSEY, CHAPTER OF ACR
Secretary, Dr. Sidney Ketyer, St. Elizabeth Hosp., 225 Williamson St., Elizabeth, N. J. 07207. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

RADIOLOGICAL SOCIETY OF RHODE ISLAND, CHAPTER OF ACR
Secretary-Treasurer, Dr. Daniel J. Hanson, 116 Nayatt Rd., West Barrington, R. I. 02806.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary-Treasurer, Dr. Marshall Rowen, Dept. Radiol., St. Joseph Hosp., 1100 Stewart Dr., Orange, Calif. 92668. Meets three times a year, usually October, February and May.

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Donald P. King, 218 Gun Club Rd., Richmond, Va. 23221. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary-Treasurer, Dr. Kenneth E. Robinson, 1441 East Avenue, Rochester, New York 14610. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Lorenz R. Wurtzebach, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 2–4, 1973.

SAN ANTONIO-CIVILIAN MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Robert M. Maurer, Santa Rosa Medical Center, San Antonio, Tex. 78207. Meets third Wednesday of each month at Fort Sam Houston Officers' Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY
President, James R. Collins, 340 Fourth Ave. Suite 15, Chula Vista, Calif. 92010. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. James G. Moore, Mary's Help Hospital, 1900 Sullivan Ave., Daly City, Calif. 94015.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

SECTION ON RADIOLOGY, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

SECTION ON RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Mario A. Calonje, 1514 Jefferson Highway, New Orleans, La. 70121. Annual Meeting.

SECTION ON RADIOLOGY, TEXAS MEDICAL ASSOCIATION
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

SOCIETY FOR PEDIATRIC RADIOLOGY
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027. Annual meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 23–24, 1973.

SOCIETY OF GASTROINTESTINAL RADIOLOGISTS
Secretary-Treasurer, Dr. Wm. B. Seaman, The Presbyterian Hospital, Columbia-Presbyterian Medical Center, 622 W. 168th St., New York, N. Y. 10032.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Dr. E. James Potchen, Edward Mallinckrodt Institute of Radiology, 660 S. Euclid Ave., St. Louis, Mo. 63110. *Administrative Officer*, Mrs. Margaret Glos, 211 E. 43rd St., New York, N. Y. 10017. Annual meeting: Americana Hotel, Miami Beach, Fla., June 12–15, 1973.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. A. D. Benjamin, 596 Carroll St., Sunnyvale, Calif. 94086. Meets the 2nd Monday of each month at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

SOUTH CAROLINA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Association meeting in May. Annual fall scientific meeting at time and place designated by the president.

SOUTH COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. James T. McClintock, P.O. Box 837, Santa Barbara, Calif. 93102. Meets fourth Monday of the month, Oct. through May.

South Dakota Radiological Society, Chapter of ACR
Secretary, Dr. M. F. Petereit, 2416 S. Phillips, Sioux Falls, S. D. 57105. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. John Byfield, 1000 West Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 7544, Mobile, Ala. 36607.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Carl T. Stubblefield, Bedford County Hospital, Columbia, Tenn. 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas State Radiological Society, Chapter of ACR
Secretary, Dr. Herman C. Sehested, 815 Medical Tower, Room 100, 1550 W. Rosedale St., Fort Worth, Tex. 76104. Annual meeting.

The Fleischner Society
President, Dr. Robert G. Fraser, 1555 Summerhill Ave., Montreal 109, P.Q., Canada. Annual meeting.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John F. Stucki, Department of Radiology, McKay-Dee Hosp., 3939 Harrison Blvd., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society, Chapter of ACR
Secretary, Dr. J. Lorimer Holm, R.R.#3, Barre, Vt. 05641.

Virginia Chapter of ACR
Secretary-Treasurer, Dr. James S. Redmond, Suite 7, Medical Center, Lynchburg, Va. 24501. Next Meeting: Nov. 6, 1972 at the Conference Ctr., Williamsburg, Va.

Washington, D. C., Chapter of ACR
Secretary-Treasurer, Dr. Albert M. Zelna, 9110 Seven Locks Rd., Bethesda, Md. 20014.

Washington State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John N. Roehr, 1011 Medical Dental Bldg., Seattle, Wash. 98101.

West Virginia Radiological Society. Chapter of ACR
Secretary-Treasurer, Dr. Andrew W. Goodwin, II, 200 Med. Arts Bldg., Charleston, W. Va. 25301. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Max C. King, 314 Woodland Hills Rd., White Plains, N. Y. 10603. Meets on second Tuesday of October, December, February and May.

Wisconsin Radiological Society. Chapter of ACR
Secretary-Treasurer. Dr. Marvin L. Hinke. 630 S. Central Ave., Marshfield, Wisc. 54449. Meets twice a year, May and September.

Wisconsin Society of Therapeutic Radiologists
Secretary. Dr. Robert W. Edland, Gundersen Clinic, LaCrosse, Wisc. 54601. Meets quarterly.

Wyoming Radiological Society, Chapter of ACR
Secretary, Dr. Ross J. Collie, Box 96, Lander, Wyo. 82520. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costarricense de Radiología
Secretary, Dr. Jorge Vargas Segura, Apartado 5367, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá
Secretary-General, Dr. Francisco Mirambell, Apartado 3352, San José, Costa Rica, Central America.
Meets annually in a rotating manner in the six countries.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad de Radiología de El Salvador
Secretary, Dr. Carlos Mejia, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D.F., México.
Secretary-General, Dr. Jorge Cano Coquí. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Heriberto Pagán Sáez, Box 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Moyne, 121 Boul. Taschereau, Greenfield Park, P.Q., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. T. Kerr, 32 Welbeck St., London, W1M/7PG, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics
Honorary Secretary-Treasurer, Dr. R. G. Baker, Ontario Cancer Foundation, Ottawa Civic Clinic, 1053 Carling Ave., Ottawa 3, Ont., Canada.

Canadian Association of Radiologists
Honorary Secretary, Dr. Champlain Charest, 1555 Summerhill Ave., Montreal 109, Que., Canada. Annual meeting: Montreal, Que., Canada, March 11–17, 1973.

Edmonton and District Radiological Society
Secretary, Dr. L. A. Koller, Suite 360, Professional Bldg., 10830 Jasper Ave., Edmonton 15, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Robert Morrison, 47 Lincoln's Inn Fields, London, W.C.2, England. The scientific meetings held in January, February and March 1973 will be combined sessions with the British Institute of Radiology and the Section of Radiology of The Royal Society of Medicine.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Hon. Secretary, Dr. D. F. Canwell, 123 St. Stephens Green, Dublin 2, Ireland.

Montreal Radiological Study Club
Secretary, Dr. W. Paul Butt, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 8:15 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1 M&AE, 1 England.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Hubert Sasseville, Verdun Hospital, Montréal, P.Q., Canada. Meets every third Tuesday from October to April.

The Hospital Physicists' Association
Honorary Secretary, J. B. Massey, B.Sc., Christie Hosp. and Holt Radium Institute, Physics Department, Withington, Manchester M20 9BX, England.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

Royal College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, 147 Macquarie St., Sydney, N.S.W. 2000, Australia.

South America

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Federación Argentina de Sociedades de Radiología
Branches of the Federation are: Sociedad de Radiólogos de la Provincia de Córdoba; Sociedad Argentina de Radiología; Asociación Argentina de Radiología; Sociedad de Radiología, Radioterapéutica y Medicina Nuclear de Rosario; Sociedad de Radiología y Medicina Nuclear del Centro y Sudeste de la Provincia de Buenos Aires (Mar del Plata); Sociedad Salteña de Radiología y Medicina Nuclear; Sociedad de Radiología de Tucumán; Sociedad de Radiología del Nordeste Argentino; Sociedad de Radiología de La Plata; and Sociedad de Radiología de San Juan.
Secretary-General-Treasurer, Dr. Roberto Habichayn, Av. Colón 637, Córdoba, Argentina.

Sociedad Argentina de Radiología
Secretary-General, Dr. Armando B. de Onaindia, Santa Fé 1171, Buenos Aires, Argentina. Meets first Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Caixa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Claudio Cortés, Casilla, 13426 Santiago, Chile. Meets first Friday of each month at Av. Santa María 1810 at 7:00 P.M.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Rodrigo Caro Molina, Cali, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología
Secretary, Dr. Carlos Palau Jimenez, Casilla 5469, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Hugo Volpe Rios, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dr. Miguel Chiappori Cambana, Av. General Santa Cruz No. 315, Miraflores, Lima, Perú, Casilla Correo, 2306, Lima, Perú. Meets monthly except during January, February, and March.

Sociedad de Radiología del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología del Nordeste Argentino
Secretary-General, Dr. Francisco J. Velar, Catamarca 561, Corrientes, Argentina.

Sociedad de Radiología de La Plata
Secretary, Dr. Hiram D. Haurigot, Calle 50 No. 374, La Plata, Argentina.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Manuel Gonzáles Maseda, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad de Radiología, Radioterapéutica y Medicina Nuclear, de Rosario
Secretary-General, Dr. Federico Frágola, Santa Fe 1798, Rosario, Argentina.

Sociedad Salteña de Radiología y Medicina Nuclear
Secretary, Dr. Julio Luis Baldi, Av. Sarmiento 536, Salta, Argentina.

Sociedad Venezolana de Radiología y Medicina Nuclear
Secretary-General, Dr. Salvador Itriago Borgas, Apartado Postal 9213, Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
Secretary, Dr. Ernst Kotcher, Wiener Allgemeine Poliklinik Mariannengasse 10, A-1090 Wien, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. The 1973 Annual Meeting is a joint meeting with the Deutsche Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Secretary, Dr. P. Hicken, The Children's Hosp., Ladywood Middleway, Birmingham B16 8ET, Great Britain. Tenth Annual Meeting, Birmingham, April 11–13, 1973.
Permanent Secretary, Clément Fauré, Hôpital des Enfants-Malades, 149, rue de Sèvres, 75 Paris 15e, France.

Société Française de Radiologie Médicale, Médecine Nucléaire et Electrologie, and its branches: Société du Sud-Ouest, du Littoral méditerranéen, du Centre et Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et du Massif Central. Parent Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Société Française de Neuroradiologie
Secretary-General, Professeur agr. R. Djindjian 16, rue de l'Université 75, Paris 7e, France. Annual meeting.

Československá Radiologická Společnost
Secretary, Associate Professor Jaromír Kolář, M.D., Sc.D., Radiological Clinic, Praha 2, U nemocnice 2, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Walter Frommhold, Director of Medizinisches Strahleninstitut der Universität Tübingen, Röntgenweg 11, 7400 Tübingen, Germany.

The 1973 Annual Meeting is a joint meeting with the Österreichische Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Società Italiana di Radiologia Medica e Medicina Nucleare
Administrative Secretary, Prof. E. Conte, Ospedale Mauriziano, 10128 Torino, Italy. Meets annually.

Societas Radiologica Danica
Secretary, Dr. Bent Langefeldt, Tretommervej 20a, DK-8240 Risskov, Denmark.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. J. D. Mulder, Dept. of Rad., Akademisch Ziekenhuis, Leiden, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Dr. José Bonmatí, Villanueva, 11, Madrid 1, España. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Sociedade Portuguesa de Radiologia e Medicina Nuclear
Secretary-General, Dr. Luís Aires de Sousa, Av. Elias Garcia, 123- 1, Esg.-Lisboa i-Portugal.

Schweizerische Vereiningung für Radiologie, Nuklearmedizin und Strahlenbiologie (Association Suisse de Radiologie, Médecine Nucléaire et de Radiobiologie)
Secretary, Dr. med. Gustav Schoch, Bethesdaspital, Gellerstrasse 144, 4000 Basel, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. L. R. Parthasarathy, 44 Constable Road, Madras—23, India.

Indonesian Radiological Society
Secretary, Dr. Gani Iljas Sasmitaatmadja, Radiology Dep., Faculty of Medicine, University of Indonesia, Salemba 6, Djakarta, Indonesia.

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month. Third National Iranian Congress of Radiology: Isfahan, Iran, May 5–10, 1973. Deadline for acceptance of papers Feb. 20, 1973.

Israel Radiological Society
President, Dr. I. Izkovitch, 2 Wingate Ave., Beit Harofe, Haifa, Israel.

Japanese American Radiological Society
Secretary, Thomas J. Imray, Maj. MC, Chief, Radiol. Dep., US Army Hosp., Camp Zana, Japan, APO San Francisco, Calif. 96343. Meets 3rd Thursday, monthly at various locations in Tokyo.

Philippine College of Radiology
Secretary-Treasurer, Dr. Edmundo V. Villacorta, Box 1284, Commercial Center, Makati, Rizal D-708, Philippines. Meets every 3 weeks on Fridays. Annual convention.

Radiological Society of Thailand
Secretary, Prof. Rojana Suvansuthi, M.D., Ph.D., Depart. of Rad., Sirizaj Hospital, Faculty of Medicine, Mahidol University, Bangkok 7, Thailand.

Africa

Association of Radiologists of West Africa
Honorary Secretary, Dr. T. M. Kolawole, University College Hospital, University of Ibadan, Ibadan, Nigeria.

Radiological Society of South Africa
Secretary, Dr. B. Rosenberg, P.O. Box 3200, Johannesburg, South Africa.

South African International Radiological Congress
Director, Dr. Paul Sneider, P.O. Box 4878, Johannesburg, South Africa.

ABSTRACTS OF RADIOLOGIC LITERATURE

E. FREDERICK LANG, M.D., Editor

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ROENTGEN DIAGNOSIS

HEAD

ARDRAN, G. M., and KEMP, F. H. The tongue and mouth in acromegaly. *Clin. Radiol.*, Oct., 1972, *23*, 434–444. (From: Nuffield Institute of Medical Research, Oxford, England.)

The roentgenographic signs of a relatively large tongue are: with the jaw closed the tongue fills the mouth cavity; the tongue may protrude through the teeth or both teeth and lips; the hyoid bone is below its usual position, which is parallel to the lower border of the mandible with the tips of the greater cornua in line with the anterior borders of the vertebrae close to the disk between the third and fourth cervical bodies; the pharyngeal airway is less than half the diameter of the trachea; the epiglottis is tipped backward with obliteration of the valleculae; the mandible lies more forward in relation to the spine than average; during swallowing the hyoid bone is not elevated to the lower border of the mandible, as occurs in the normal; and there is usually a small residue in the mouth after swallowing.

The commonest feature of acromegaly after increase in the size of the extremities is enlargement of the tongue. In 581 cases it was large in 95 per cent of the individuals. In addition, the soft palate and the tonsils may be large. These features may be compensated for in acromegaly by incomplete closure of the jaws during rest and by maintaining the mandible in a position of forward displacement to provide an adequate airway.

The authors studied 6 acromegalic patients clinically and roentgenographically and examined the roentgenograms of an additional 17 patients who had been seen in the previous 32 year period. They noted that there was considerable variation in growth of different parts of the mandible, suggesting that all parts of the mandible do not respond to pituitary hormone. The alveolar processes were irregularly enlarged with most growth in the incisor region and least in the molar region. The mandibular rami were frequently normal or shorter than average. The possibility that the enlargement of the tongue influences the size and shape of the jaws in acromegaly is considered.

Since extraction of teeth may result in reduction of the size of the mouth cavity, this operation may be of considerably greater significance in acromegaly than in normal individuals.—*E. Frederick Lang, M.D.*

CONWAY, JAMES J., and VOLLERT, JEANETTE M. The accuracy of radionuclide imaging in detecting pediatric dural fluid collections. *Radiology*, Oct., 1972, *105*, 77–83. (Address: James J. Conway, M.D., Department of Radiology, The Children's Memorial Hospital, 2300 Children's Plaza, Chicago, Ill. 60614.)

The discrepancy between the detection rate of dural fluid collections in adults (80 per cent), and in children (60 per cent), by radionuclide imaging techniques afforded the stimulus for this study. The literature reviewed between 1965–1971 revealed only a 67 per cent detection rate in more than 1,176 children so examined. Possible causes of poor detection and false positive interpretation are discussed.

From January 1968 through June 1970, 795 brain imaging studies were performed with parenteral Tc 99m pertechnetate (100 μc/lb.) at Children's Memorial Hospital. Oral $KCLO_4$ was given to block the choroid plexus prior to imaging by the following schedule: 150 mg.—up to 1 year of age; 300 mg.—ages 1 through 4; and 450 mg. after 4 years of age. Gamma camera images in anterior, posterior, vertex, and both lateral positions were routinely made 30 minutes postinjection. Since 1970, rectilinear scan images are made anteriorly, posteriorly, and bilaterally 2 hours postinjection. Additional images and maneuvers are employed, as necessary.

The criterion of correlation was at least 2 ml. of fluid recoverable from the dural space by subdural tap, burr hole, craniotomy, or autopsy. Twenty-five of the cases with radionuclide images met the criterion. There were: 20 subdural hematomas or effusions; 4 subdural empyemas; and 1 epidural hematoma. Eighteen cases were bilaterally involved, and only 7 were unilateral. Of the false-negative results, 8 of 10 were from the category of bilateral involvement. The other 2 were an acute subdural hematoma in a hemophiliac and "a small subdural hygroma." Several in the true-positive group of bilateral involvement had asymmetric collections. The presence of membranes associated with the dural collection was verified in only 8 of the 25 cases.

The nature of the radionuclide image is such that it should readily lend itself to the detection of this abnormality. This seems so in adults where 85 per cent of the collections are unilateral, and the detection rate is 80 per cent. In early life subdural bleeding is 80–85 per cent bilateral, and presents a symmetric image unless the loculations are truly unequal. Symmetrically increased bands of radioactivity over the periphery of the image may be created by many diverse conditions. Timing is important; the detection rate increases significantly 7–10 days post trauma, and also with images which are rendered later than the usual 30 minute postinjection sequence (2–3 hours). Historic and clinical correlation is also important, for dural fluid accumulations are more prevalent post trauma, post meningitis, and following "normal birth." The one who is to render the interpretation should attend

the performance of the procedure, study the clinical material, examine the patient, and correlate with radiographic studies when indicated.

Although the yield may seem small, when the procedure is performed properly and interpreted carefully, it may be of immeasurable value in the management of a particular case.—*F. C. Petty, M.D.*

GENITOURINARY SYSTEM

PINGGERA, WULF F., and POPOVTZER, MORDECAI M. Uremic osteodystrophy: the therapeutic consequences of effective control of serum phosphorus. *J.A.M.A.*, Dec., 1972, *222*, 1640–1642. (From: Department of Medicine, University of Colorado Medical Center, Denver, Colo.)

Uremic osteodystrophy is a frequent complication in patients undergoing hemodialysis for a prolonged period. Frequently this is clearly secondary hyperparathyroidism; and elevated levels of parathyroid hormone may be observed even in patients with mild impairment of renal function. The pathogenesis of secondary hyperparathyroidism is not well understood. Acquired resistance to physiologic amounts of vitamin D, leading to a decrease in ionized calcium has been suggested; and another suggestion is retention of phosphorus due to a decreasing nephron population, with increased serum phosphorus, decreased serum calcium, and excessive stimulation of parathyroids. The authors have investigated the effect of restoration of serum calcium to normal levels.

A 27 year old man gradually developed subcutaneous masses of calcification at the wrists, in the hands, in the shoulder, and in the foot, in a period of 3 years following the beginning of a twice-weekly chronic hemodialysis program. The calcified masses became clinically incapacitating and because of this the patient was readmitted for hospitalization. The concentration of calcium in the dialysate was increased from 5 to 6 mg./100 ml., and dried aluminum hydroxide gel was administered orally at the rate of 24 gm./day. After 6 weeks there was marked clinical improvement, and there was striking roentgen evidence of decrease in the size and density of the calcified subcutaneous masses. In addition, healing of subperiosteal resorption was observed. Decrease in both serum calcium and serum phosphorus concentrations occurred.

Five months later the patient discontinued the aluminum hydroxide for 5 weeks. The subcutaneous masses which previously had shown almost complete regression increased again in size and the patient became handicapped as before. Reinstitution of the administration of aluminum hydroxide resulted 4 weeks later in marked improvement with resolution of soft tissue calcification, improvement in the osteitis fibrosa as shown by roentgen studies, and clinical improvement. Eight weeks after starting the treatment there was almost complete disappearance of the soft tissue calcifications.

Throughout the study the levels of magnesium in the dialysate and the serum remained constant, and this suggests that magnesium did not play a part in the regression of the soft tissue calcification. The authors recognize the danger of the development of hypercalcemia and osteomalacia due to severe phosphate depletion in the presence of large doses of aluminum hydroxide. Nevertheless, they suggest its use in combination with the high calcium concentration of the dialysate.

Subtotal or total parathyroidectomy has been successful in most cases of osteitis fibrosa in the presence of chronic renal failure.—*E. Frederick Lang, M.D.*

SMITH, PATRICK J. B., WILLIAMS, R. E., and DEDOMBAL, A. T. Genito-urinary fistulae complicating Crohn's disease. *Brit. J. Urol.*, Dec., 1972, *44*, 657–661. (From: Department of Urology, Leeds, England.)

A genitourinary fistula may occur in patients with Crohn's disease at any age and at any stage of the disease process. The first case was reported in 1936, 4 years after the original description of Crohn's disease. In reported series the incidence varies between 1 and 8.5 per cent with an incidence of 1.6 per cent in the largest reported series. In the present series of 332 patients there were 14 fistulae with an incidence of 4.2 per cent. The usual fistula involves the ileum and bladder; and occasionally the colon is involved as well. Ileovaginal fistula is rare. In these patients the symptoms of the original disease had been present between 3 months and 20 years before the development of the fistula, and in 4 cases the occurrence of the fistula was the presenting feature.

The most successful form of investigation for establishing the diagnosis of fistula was cystoscopy. Barium studies were not very helpful in recognition of the fistula, although they did aid in diagnosis of the underlying abnormality. The changes in the bladder are typically localized to the vault and vary from slight reddening of the mucosa to edematous polypoid change or, rarely, observation of fistulous tract. It is usual that the lesion is localized and other portions of the urinary tract are not involved, except by infection.

Treatment is surgical with primary closure of the urinary tract epithelium. This was successful in 11 out of 14 cases. In 3 the fistula recurred, but all 3 responded to a second operation.—*E. Frederick Lang, M.D.*

CAYTEN, C. GENE, DAVIS, ARNOLD V., BERKOWITZ, HENRY D., and ROBERTS, BROOKE. Ruptured abdominal aortic aneurysms in presence of horseshoe kidneys. *Surg., Gynec.*

& Obst., Dec., 1972, *135*, 945–949. (From: Department of Surgery and Harrison Department of Surgical Research, University of Pennsylvania School of Medicine, and Hospital of the University of Pennsylvania, Philadelphia, Pa.)

The rare association of abdominal aortic aneurysm and horseshoe kidney has been reported 23 times, and ruptured aneurysm in the presence of this anomaly has been reported once. The present article describes 2 additional patients with ruptured abdominal aortic aneurysm and a third with an unruptured aneurysm associated with a horseshoe kidney.

The association of abdominal aortic aneurysm and a horseshoe kidney is probably a chance phenomenon. All but 1 of the recorded patients have been male and the mean age is 61 years. The fusion of the lower poles and the usually anomalous blood supply of the kidney make exposure and repair difficult. In addition to anomalies in number, anomalies in position and drainage of the vessels occur, making great care in identification of the vessels important.

In the 20 reported patients with unruptured aneurysm in whom resection was carried out in the presence of horseshoe kidneys, there has been only 1 operative death. It is probably no longer justifiable to withhold operation because of the added complexity. Arteriography should be performed prior to all elective resections when a horseshoe kidney is suspected. If it is unsuspected, operative arteriography has been suggested when the aneurysm is unruptured. It is frequently possible to mobilize the kidney sufficiently to obviate division of the isthmus.—*E. Frederick Lang, M.D.*

Thornbury, John R. Needle aspiration of avascular renal lesions: correlation of contrast medium injection with cytologic and arteriographic diagnoses. *Radiology*, Nov., 1972, *105*, 299–302. (From: Department of Radiology, University of Michigan Medical Center, Ann Arbor, Mich.)

Needle aspiration and arteriography can be considered complementary procedures in evaluation of avascular renal lesions. Where diagnostic error may result from one procedure, the other may provide the correct diagnosis.

The author correlates the diagnostic results from 53 needle aspirations of avascular renal lesions in a series of 50 patients with diagnoses from selective renal arteriography. False positive and false negative diagnoses occurred in a small number of cases from use of either procedure.

If clear yellow fluid was aspirated and the injected contrast material showed a reasonably smooth lining in a thin-walled cystic lesion, the diagnosis of benign cyst was made. If aspiration produced little fluid or dark turbid fluid and the contrast material showed dispersion into tissue, a diagnosis of tumor was made. Cytologic study of a sample of the aspirate was reported as positive or negative for malignancy. Arteriographic diagnoses ranged from benign cyst through suspicion of malignancy to malignant tumor.

Diagnostic errors in needle aspiration resulted from improper needle placement and a previously "bled into" cyst simulating a tumor. Cytologic examinations and arteriography provided the correct diagnosis of benign cyst in each case.

The choice between these 2 roentgenographic procedures should be related to the most likely diagnosis, indicated by the clinical setting and the angiographic evidence. If the presumptive diagnosis is benign cyst, then needle aspiration is the first diagnostic procedure selected.

If the most likely diagnosis is tumor, then renal arteriography should be the procedure of choice. If an avascular lesion is found, the needle aspiration should be performed to rule out the possibility of a necrotic renal malignancy. Most commonly, aspiration will provide a diagnosis of benign cyst in these circumstances and surgery will not be necessary.

Explanations for false positive and false negative diagnosis in both procedures are discussed as well as the controversial aspects of needle aspiration and cytology.—*J. L. Montgomery, M.D.*

Escudero Barrilero, A., Sebastián Borruel, J. L., Martín, Lopez, San Martín, P., Hitos, E., and M.-Piñeiro, J. A. Pseudotumorales renales. (Renal pseudotumors.) *Arch. españ. urol.*, July–Aug., 1972, *25*, 425–438. (From: Servicio de Urología, Residencia Sanitaria de la Seguridad Social "La Paz," Bolivia.)

Three cases of congenital hypertrophy of Bertin's columns are reported.

This entity, which is of no pathologic significance, produces pyelographic and nephrotomographic changes indistinguishable from those due to a true neoplasm; arteriography is necessary for differential diagnosis.

It occurs more frequently in kidneys with duplicated pyelocalyceal structures. In itself, this is a nonsymptomatic condition, but it is important because of the more serious conditions it simulates roentgenographically.—*Julian B. Alvarez, M.D.*

Llopis Mínguez, B., Baixauli Martínez, J., Valls Blasco, F., San Juan de Laorden, C., Maset Maldonado, J., and Simó, Oleza. Ureteritis quistica. (Ureteritis cystica.) *Arch. españ. urol.*, May–June, 1972, *25*, 349–362. (From: Servicio de Urología, Ciudad Sanitaria de la Seguridad Social "La Fe," Valencia, Spain.)

The authors report a case of unilateral cystic

uropathy, localized to the upper third of the left ureter. It was incidentally discovered during surgery in a 51 year old female who was undergoing a nephrectomy (because of nonfunctioning left kidney with a staghorn calculus).

The presence of multiple submucous cysts (cystic uropathy) is believed to be the result of a chronic inflammation of the mucosa of the urinary tract. The inflammation could be infectious or mechanical in nature, the epithelial cells undergo metaplastic changes and become buried in the submucosa, then they undergo cystic degeneration. These cysts can be found anywhere along the urinary tree, but most frequently involve the upper third of the ureter and the bladder, near the ureteral orifice. The contents of the cysts are liquid or gelatinous. The changes might be bilateral.

The clinical picture of cystic uropathy is nonspecific. The cysts might be detected by pyelography. The entity is considered a benign disease, usually treated medically.—*Julian B. Alvarez, M.D.*

Carlson, David H., and Wilkinson, Robert H. Neurofibromatosis of the bladder in children. *Radiology*, Nov., 1972, *105*, 401–404. (Address: David H. Carlson, M.D., Newton-Wellesley Hospital, Newton, Mass. 02158.)

Three cases of neurofibromatosis of the bladder in children are reported. Nine previously reported cases are also discussed. The authors indicate that the children presented with either multiple symptoms or none at all.

Neurofibromatosis, as described by von Recklinghausen in 1882, is a hamartomatous disorder of neural crest derivatives. Urinary tract involvement is rare.

Neurofibromas are not usually palpable abdominally until they reach a great size. The authors emphasize the fact, therefore, that rectal examination in evaluation of bladder neurofibromas is very important.

Of the authors' 3 cases, all had café-au-lait spots and 2 had cutaneous masses at some time.

Cutaneous neurofibromas are not common in children; therefore, the presence of skin pigmentation and a bladder mass in a child should create a high index of suspicion.

The authors describe each of their 3 cases in some detail indicating the type of management for each. It is stated that 12 per cent of cases of generalized neurofibromatosis undergo malignant transformation. Of this 12 per cent, approximately 22 per cent reveal distant metastasis.—*J. P. Eberts, M.D.*

Birnholz, Jason C. Uterine opacification during excretory urography: definition of a previously unreported sign. *Radiology*, Nov., 1972, *105*, 303–307. (From: Departments of Radiology, Harvard Medical School and the Massachusetts General Hospital, Boston, Mass.)

The author reports the observation of uterine opacification following intravenous instillation of either 300 ml. of a 30 per cent methylglucamine diatrizoate solution, or 50 ml. of a 52 per cent methylglucamine, 8 per cent sodium diatrizoate solution rapidly injected. This previously unreported phenomenon is termed an adventitious hysterogram.

Nineteen unequivocal examples of soft tissue opacification were identified. In these 19 examples, 5 were proved by surgical excision with examination revealing typical uterine leiomyomas both grossly and on histologic evaluation. Of the remaining 14 cases, 6 were thought to have enlarged uteri containing myomas by examining gynecologists. Another 6 women were considered to have enlarged uteri roentgenographically during the uterograms. Two women showed opacified uteri which were not enlarged. None of the last 8 had a gynecologic examination.

Uterine localization by the high dose technique is distinguished from the transient increase in roentgenographic density of the spleen and liver following high doses of contrast material. The opacification involves primarily the myometrium. The theory behind the opacification of the proved leiomyomas is that these tumors are masses of proliferating arteries. The capillary network is profuse and the interstitial space correspondingly large with draining veins at the periphery of the tumor. This, according to the author, allows passive accumulation of the contrast agent within the uterine myoma. This peculiarity correlates with the hypothesis of passive interstitial accumulation of contrast agent as the mechanism of the hysterogram in the enlarged uteri. The author, however, is uncertain as to the reason for the nature of opacification in apparently normal uteri.

The author in summary then describes the presence of an adventitious hysterogram in patients with either proved uterine myomas or enlarged uteri. He indicates the value of this opacification in the work-up of pelvic mass lesions. However, he does indicate that this is a nonspecific type of hysterogram and that additional experience is required to define the limitations.—*J. P. Eberts, M.D.*

Skeletal System

Anton, H. C. Hand measurements in acromegaly. *Clin. Radiol.*, Oct., 1972, *23*, 445–450. (From: Department of Radiology, Stobhill Hospital, Glasgow, Scotland.)

Measurements were made of portions of the hand as shown in a single dorsopalmar view in a series of 100 normal controls and 12 acromegalic patients. The sesamoid index is obtained from the medial sesamoid at the metacarpophalangeal joint of the thumb by measuring the greatest transverse diameter in mm.

and the greatest vertical diameter in mm. and multiplying these figures. The width of the distal tuft of the distal phalanx of the middle finger was measured in a similar group, the thickness of the second metacarpal phalangeal joint space was measured, and the hand lengths between the articular margin of the lower end of the radius and the tip of the distal phalanx of the middle finger were measured.

A considerable difference in sesamoid index for males and females was found. A sesamoid index of over 40 in the male and over 32 in the female strongly suggests acromegaly. A tuft breadth above 9.9 mm. was found in 6 of 7 female acromegalics. The range of normal in males is somewhat greater and the excess is more difficult to assess. The measurement in 4 of 5 male acromegalics was 11 mm. or more, but some normal males had tufts measuring 12 mm. The normal joint space width in males is 3 mm. or less and in females it is 2 mm. or less. Here, likewise, excess is more significant in females as the variation in males is greater. Hand length was used to detect cases of giantism and this was present in only 1 of the 7 females.

Generally, none of the roentgenologic signs is invariably present, and the marked quantitative sex difference is emphasized.—*E. Frederick Lang, M.D.*

Woodhouse, N. J. Y., Fisher, M. T., Sigurdsson, G., Joplin, G. F., and MacIntyre, I. Paget's disease in a 5-year-old: acute response to human calcitonin. *Brit. M. J.*, Nov., 1972, *4*, 267–269. (From: Departments of Medicine and Chemical Pathology, Royal Postgraduate Medical School, Hammersmith Hospital, London, England.)

The authors present detailed information concerning a 5 year old boy with histologic changes of adult Paget's disease. The term juvenile Paget's disease was first used to describe this unusual disorder in an 11 year old boy in 1958. Several further examples have been reported under different terms between 1956 and 1968. The disease is characterized by deformity in early life, fragile bones, and elevation of serum alkaline phosphatase and acid phosphatase levels. Urine hydroxyproline excretion is increased and isotope studies have confirmed a high bone turnover rate. Although it is usually a generalized disease, involvement of a single bone can occur.

The authors' patient underwent extended metabolic studies. These showed elevated and more or less continually rising serum acid and alkaline phosphatase levels and a high excretion of hydroxyproline in the urine. Attention was directed to the problem at the age of 1½ years after a fall with a fracture of the right femur. Seven further fractures all in the long bones occurred. All fractures healed normally. The roentgen appearance of the involved bones was characteristic of Paget's disease. A bone biopsy of the ilium showed a grossly abnormal appearance, similar to the appearance of very severe Paget's disease.

Human calcitonin was administered and resulted in pronounced reduction in bone turnover, as shown by an immediate and sustained fall in urine hydroxyproline excretion. At the same time intestinal calcium absorption increased. The aim of such treatment is to prevent further bone deformity and to reduce the excessive fragility. The satisfactory response has persisted during a 3 month period. The patient's response to injuries during this period is likewise encouraging as no further fracture has occurred.—*E. Frederick Lang, M.D.*

Bunata, Robert E., Fahey, John J., and Drennan, Denis B. Factors influencing stability and necrosis of impacted femoral neck fractures. *J.A.M.A.*, Jan., 1973, *223*, 41–44. (From: Department of Orthopedic Surgery, St. Francis Hospital, and Northwestern University Medical School, Evanston, Ill.)

Fractures of the femoral neck may be described as displaced or undisplaced. The undisplaced fracture is frequently designated impacted.

The authors feel that impaction is more apparent than real and usually does not involve actual driving together of the fragments at the time of injury. They have examined 153 impacted fractures of the femoral neck, of which they treated and followed 113. Clinically, only mild to moderate discomfort was observed with active or passive motion of the hip in patients with undisplaced or impacted fractures, while with the others significant pain and limitation were encountered. Of the total 153 fractures, only 7 were impacted in varus, and 99 were in valgus, with 29 in extreme valgus. Pauwel's angle was measured in each of the 153 patients and of these fractures the average angle was 41°.

Of the 113 cases, 53 were treated primarily with internal fixation and all healed without change in position. Sixty fractures were treated nonoperatively and 88 per cent healed uneventually, while 7 became displaced and were subsequently treated as displaced fractures. Of these 7, the average Pauwel's angle was 51° with a range between 47° and 62°. All were higher than the average angle of the 53 stable fractures. No other single fracture characteristic correlated with the incidence of fracture displacement.

Experiments have shown that complete interruption of foveal blood supply occurs when the ligamentum teres is compressed between the cartilaginous surfaces of the hip, and this occurs consistently in the position of extreme valgus. In the present series, 9 out of 153 fractures eventuated in avascular necrosis for an incidence of 16.9 per cent. The single feature which correlated with the incidence of avascular necrosis is the extreme valgus position following fracture. Analysis has shown that the association between aseptic necrosis and the valgus position is

statistically significant. Retroversion of the head showed no correlation with the presence of avascular necrosis, although this is not an acceptable position for reduction of the displaced femoral neck fracture. However, in this series, impacted fractures in this position were not unstable.

The authors conclude that the more vertical the fracture line the more likely is displacement. Further, when there are no contraindications to surgery, internal fixation with threaded pins is recommended for an impacted femoral neck fracture with a Pauwel's angle greater than 45 per cent. They feel that the presence of extreme valgus displacement is of prognostic value and are at present unable to modify this effect. They believe that reducing fractures with this displacement would probably be hazardous and unrewarding.—*E. Frederick Lang, M.D.*

RADIOISOTOPES

Castronovo, Frank P., Jr., and Callahan, Ronald J. New bone scanning agent: ^{99m}Tc-labeled 1-hydroxy-ethylidene-1, 1-disodium phosphonate. *J. Nuclear Med.*, Nov., 1972, *13*, 823–827. (Address: Frank P. Castronovo, Jr., Department of Radiology, Division of Nuclear Medicine, Massachusetts General Hospital, Boston, Mass. 02114.)

The authors describe the synthesis and quality control of 1-hydroxy-ethylidene-1, 1-diphosphonic acid (HEDPHA), and the formulation and quality control of Tc^{99m}-HEDSPA. The formulation of Tc^{99m}-labeled HEDSPA necessitates the use of tin-reduced pertechnetate, since the compound will not complex with technetium as pertechnetate.

The HEDPHA was synthesized by treating acetic acid with PCl_3. The disodium salt of HEDSPA was prepared by adjusting a known amount of the HEDPHA to pH 8.5. The Tc^{99m}-HEDSPA was prepared by adding freshly prepared stannous chloride in HCl into the HEDSPA. Freshly eluted Tc^{99m} was then added. The pH of the Tc^{99m}-HEDSPA was adjusted to 7.2–7.4 with NaOH.

The quality control procedures for Tc^{99m}-HEDSPA involved the following: descending paper chromatography with 85 per cent methanol and Sephadex Gel column chromatography. The *in vivo* distribution of the Tc^{99m}-HEDSPA was carried out in adult male Swiss-Webster mice. The pharmacodynamics of Tc^{99m}-HEDSPA was followed in young and adult rabbits.

The development of Tc^{99m}-HEDSPA is a simple "in-house" procedure for providing a chemically stable skeletal localizing agent in gram amounts. The disphosphonates are "chemisorbed" onto bone, which leads to, at most, a monomolecular layer. Chemisorption can be regarded as a zero-order reaction. King and associates investigated the dose-related effects of diphosphonates on bone formation in animals and concluded that at systemic doses of 5 mg./kg./day×28 days in dogs there were no toxic effects. Based on the minimum lethal dose of 0.2 gm./kg. of body weight in mice, the safety factor in a 70 kg. human would be 1.4×10^4.

The distribution of Tc^{99m}-HEDSPA was studied in adult mice: 49.6 per cent of Tc^{99m}-HEDSPA was present in bone at 1 hour; 55.3 per cent at 3 hours; and 54.7 per cent at 6 hours. The blood cleared quite rapidly: 4.35 per cent of the Tc^{99m}-HEDSPA was present at 1 hour; 1.02 per cent at 3 hours; and 0.08 per cent at 6 hours. There was 3.63 per cent of the Tc^{99m}-HEDSPA in the kidneys at 1 hour; 3.21 per cent at 3 hours; and 0.91 per cent at 6 hours. There was 38.7 per cent of the Tc^{99m}-HEDSPA in the bladder (urine) at 1 hour; and 39.2 per cent at 3 hours.

The ease of synthesis of the compound, its chemical stability and its ability to complex with Tc^{99m} make HEDSPA a useful skeletal imaging agent.—*Charles W. Cooley, M.D.*

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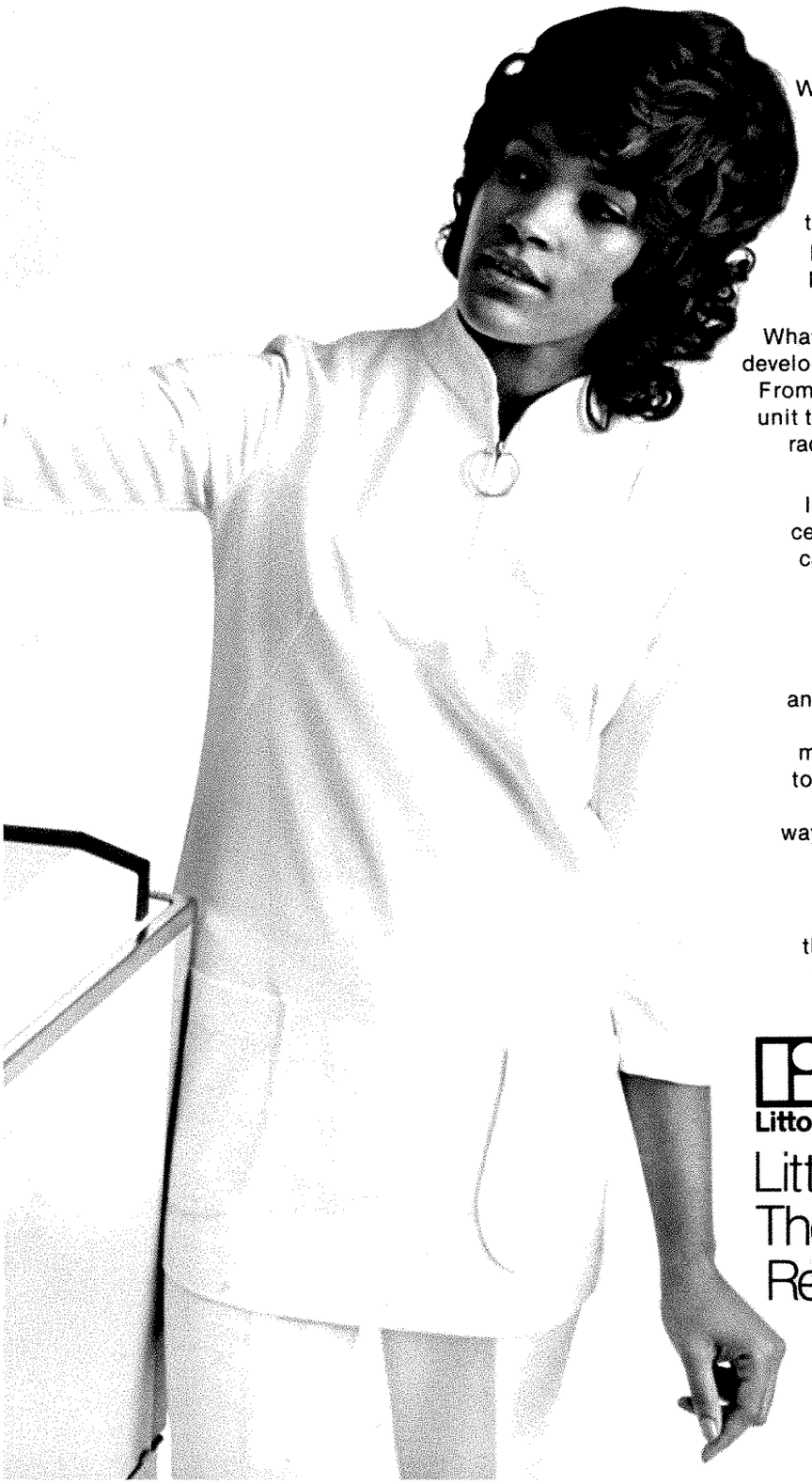
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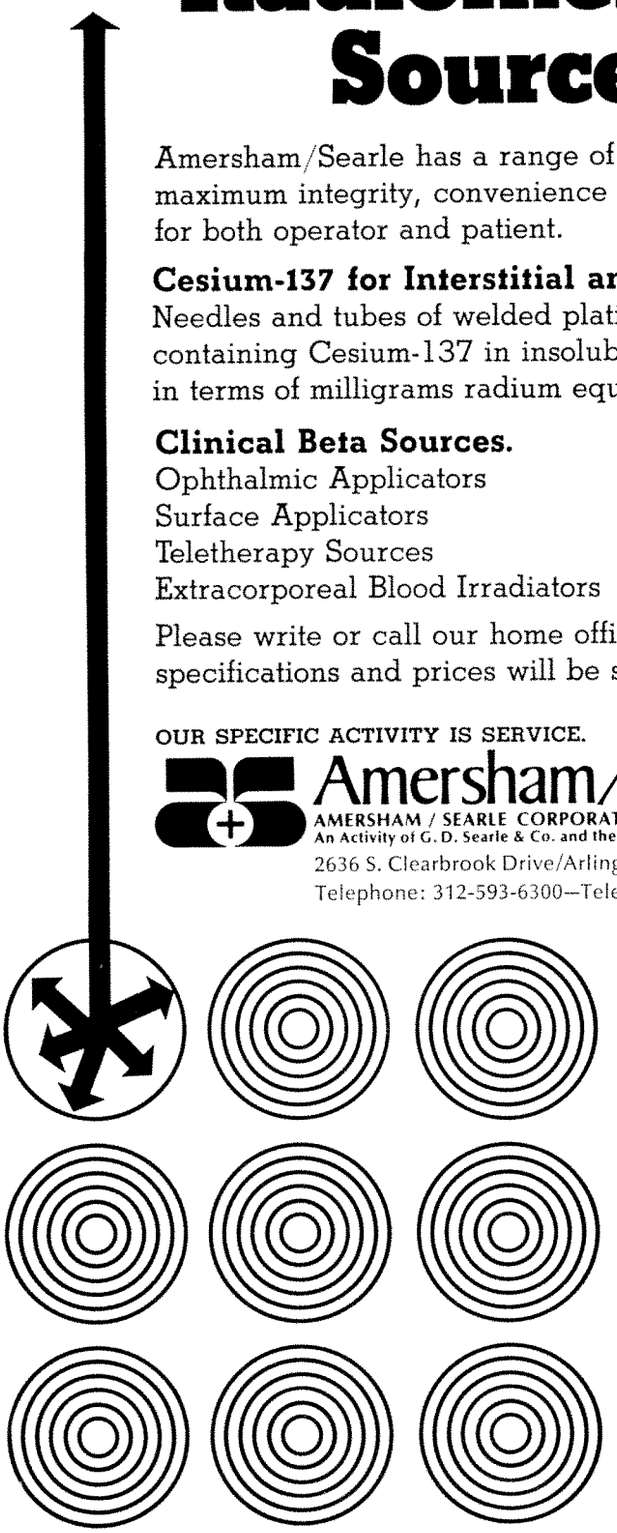
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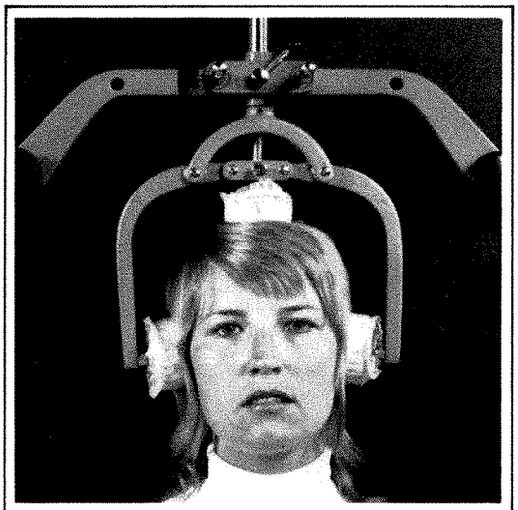
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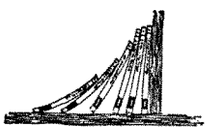
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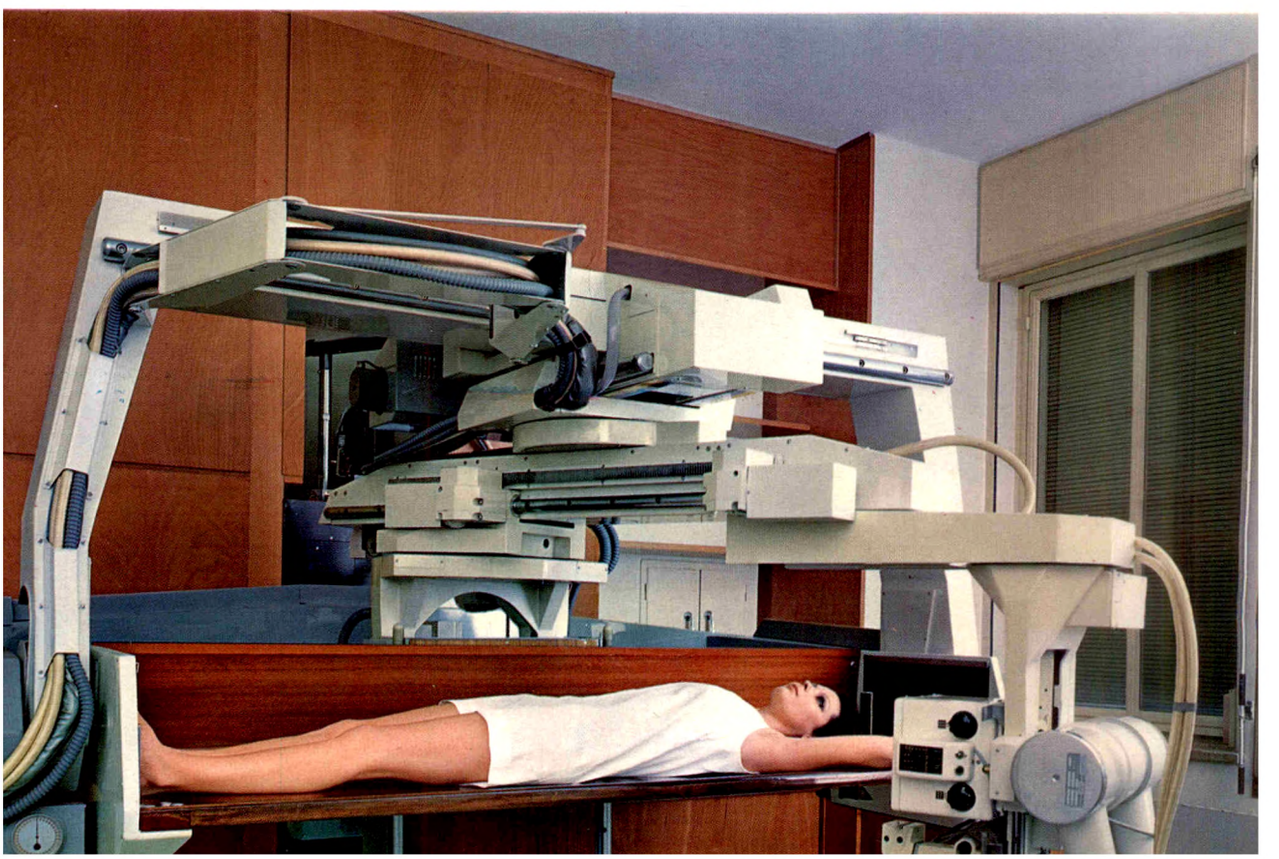
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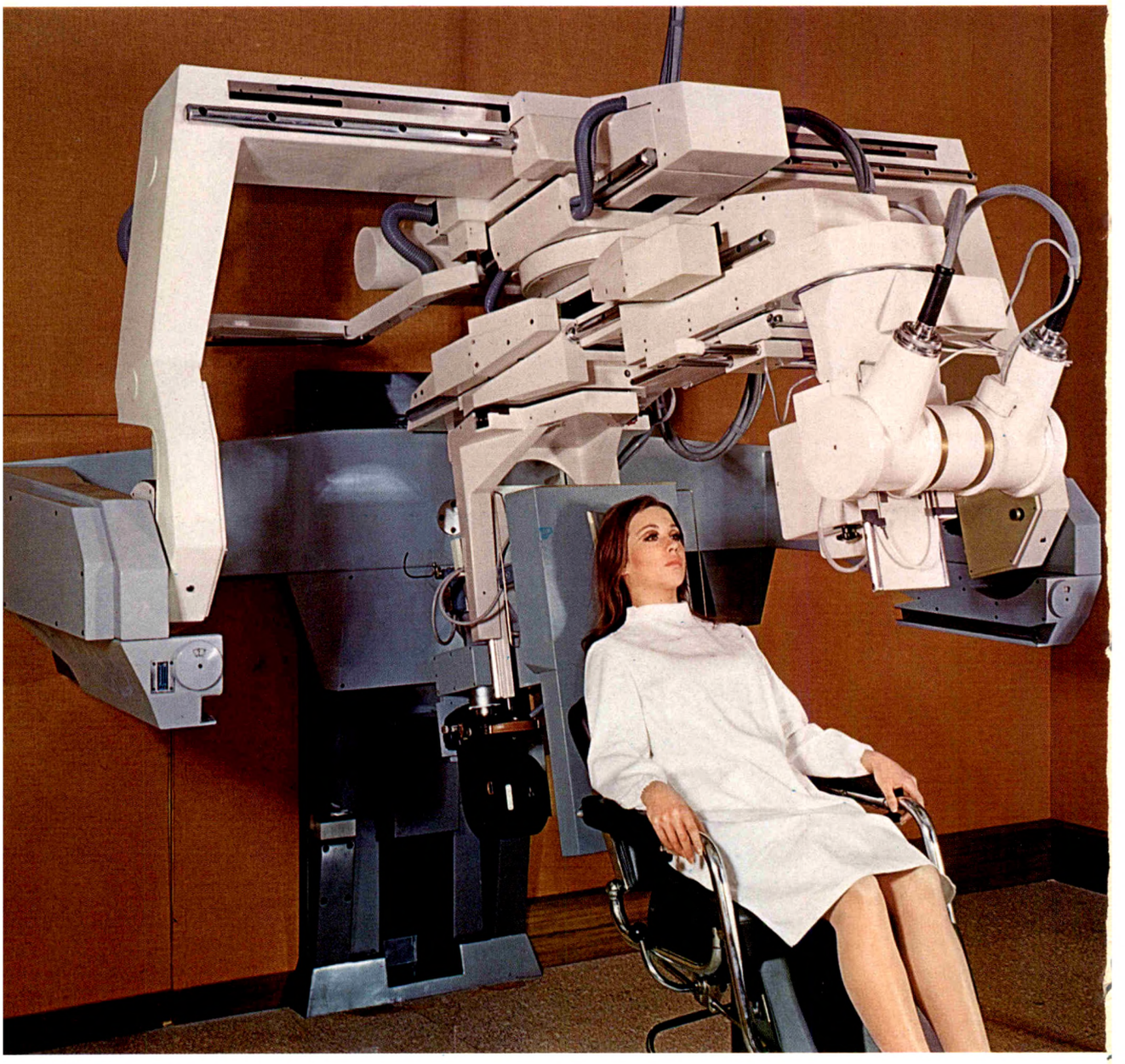


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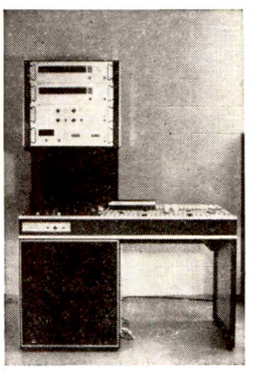
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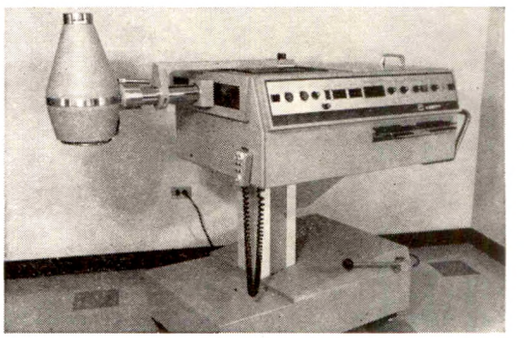
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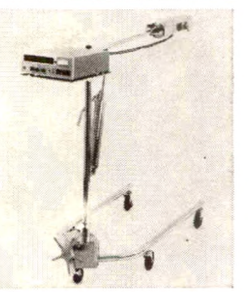
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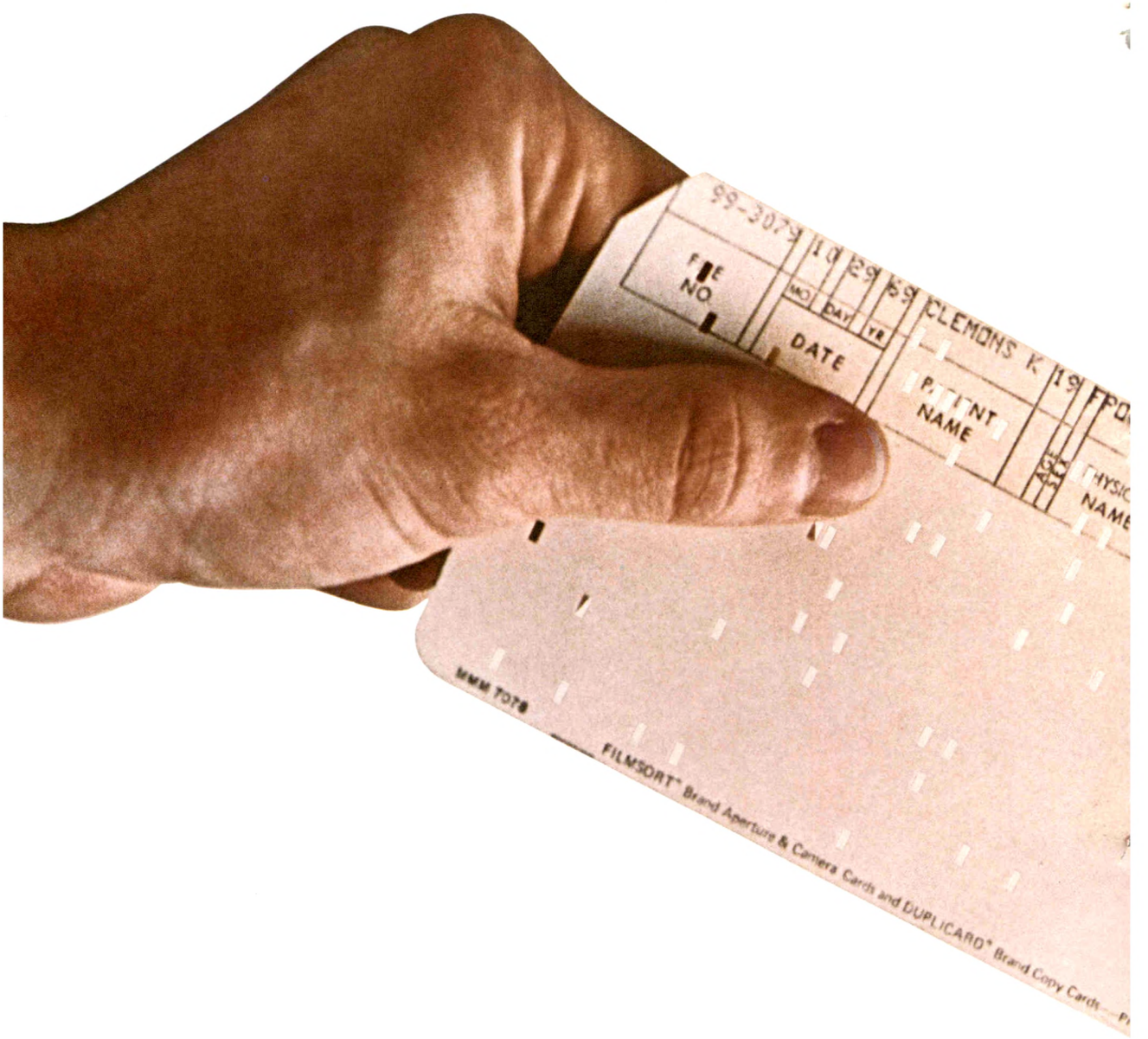
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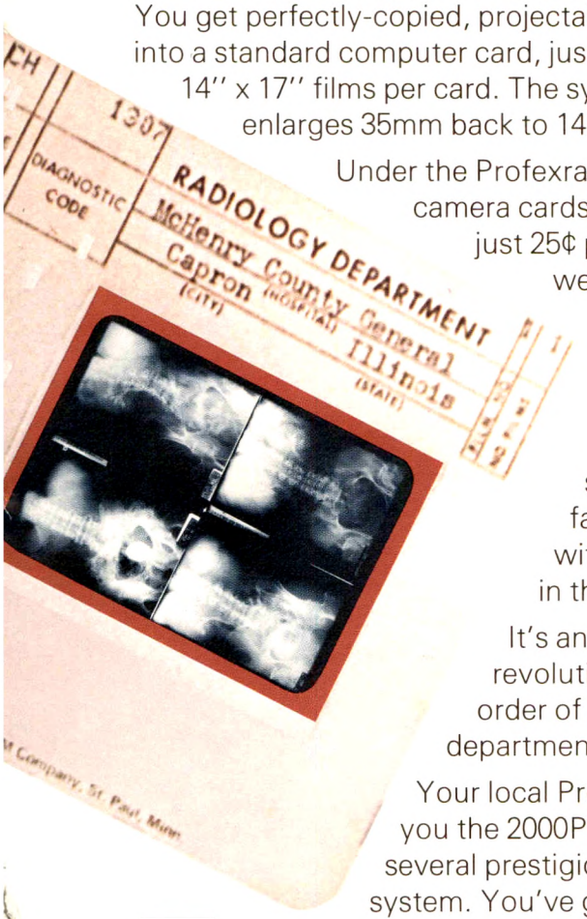
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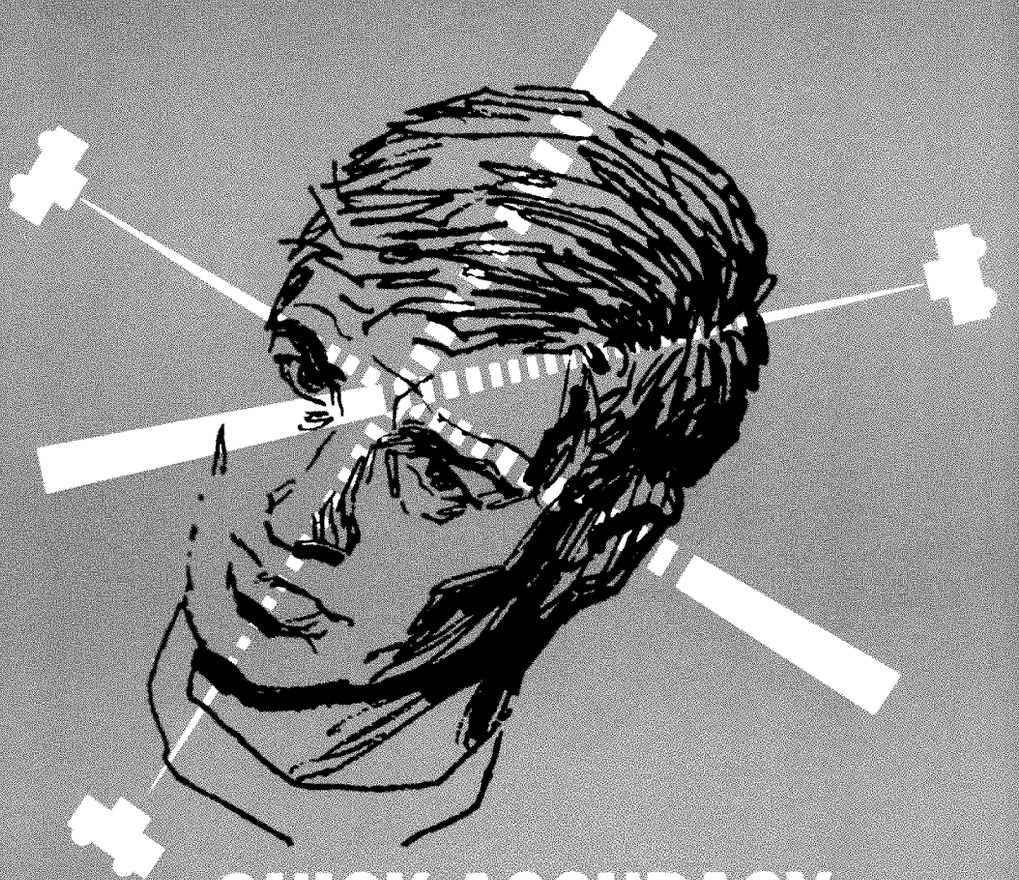
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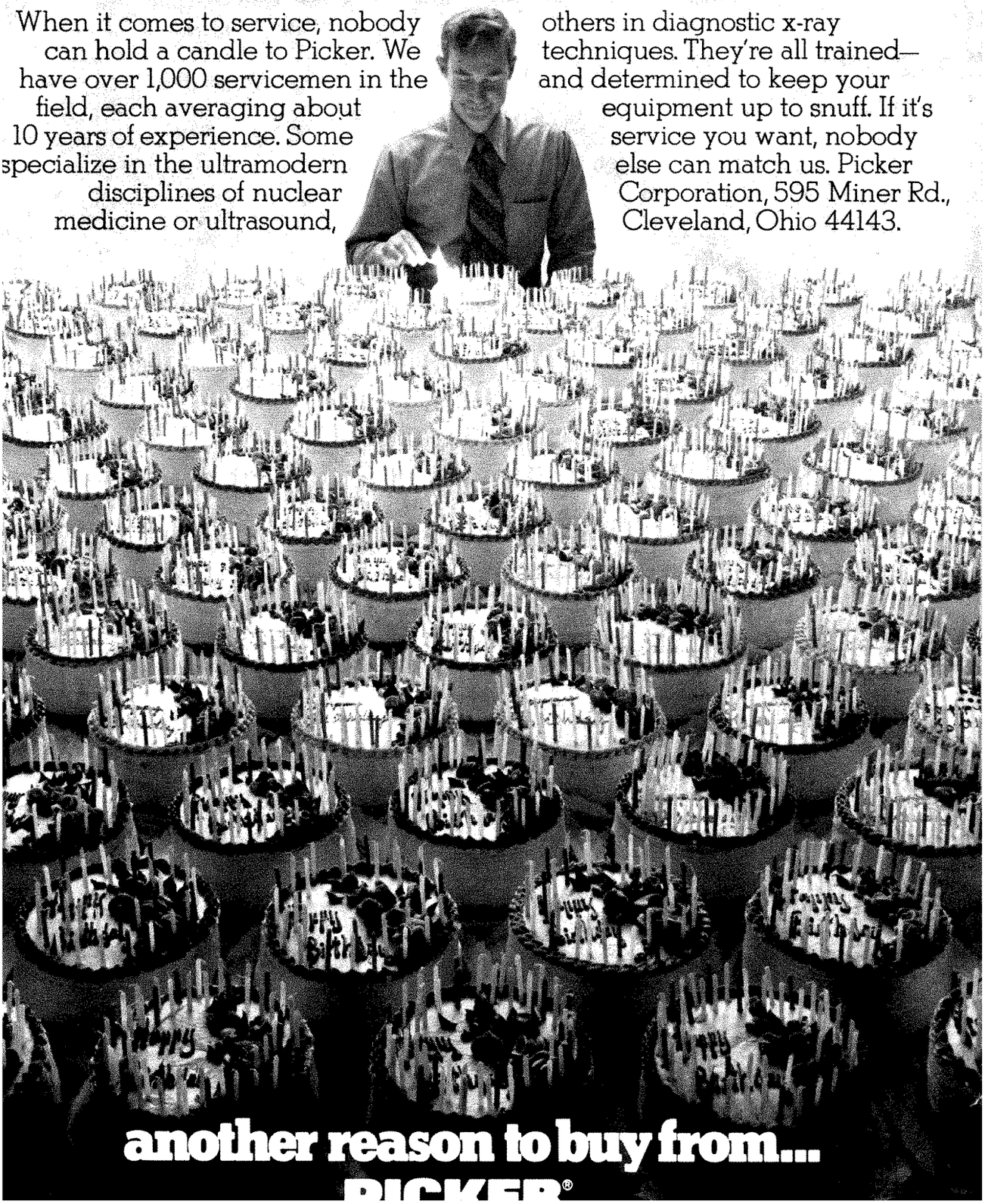
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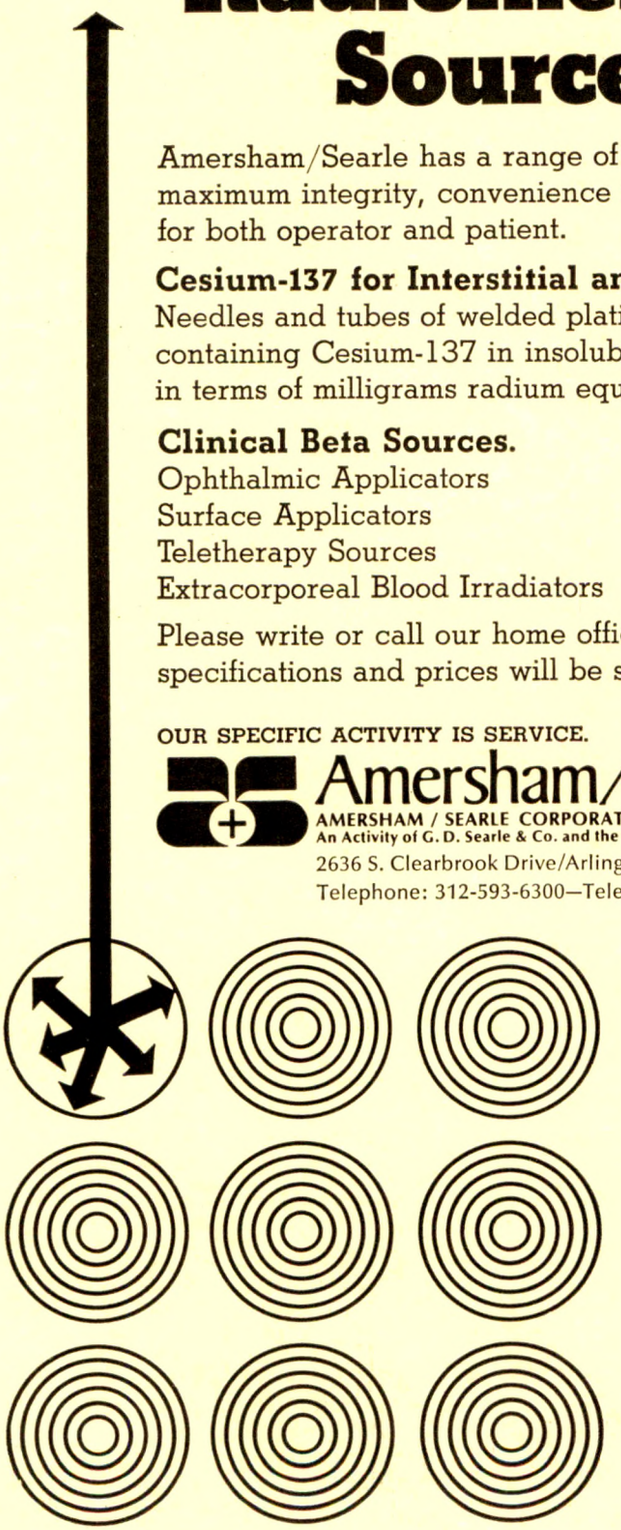
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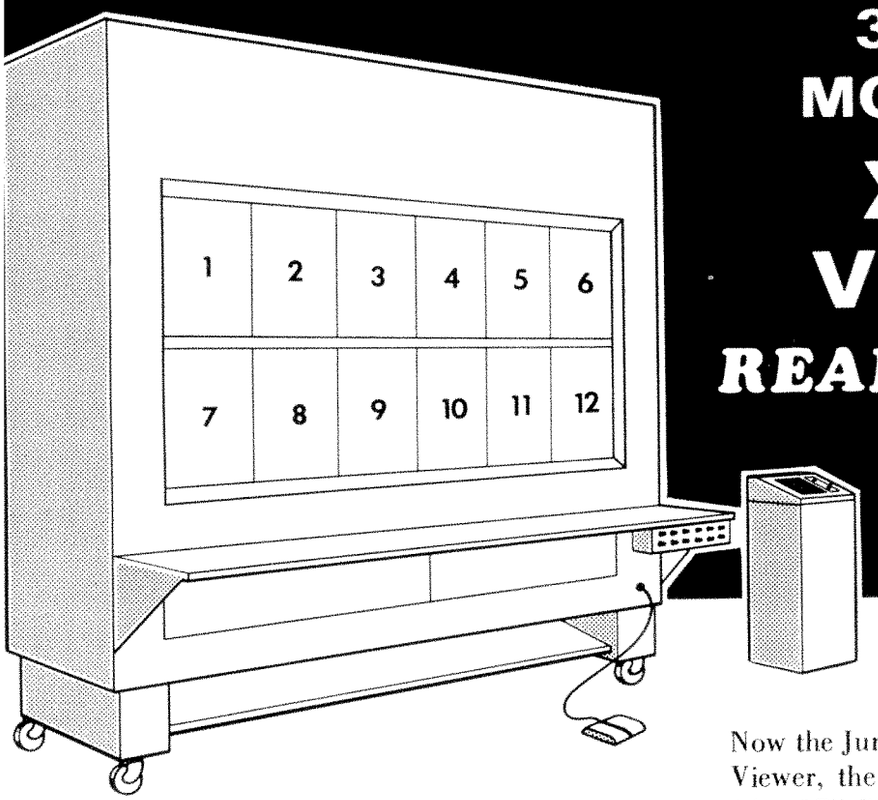
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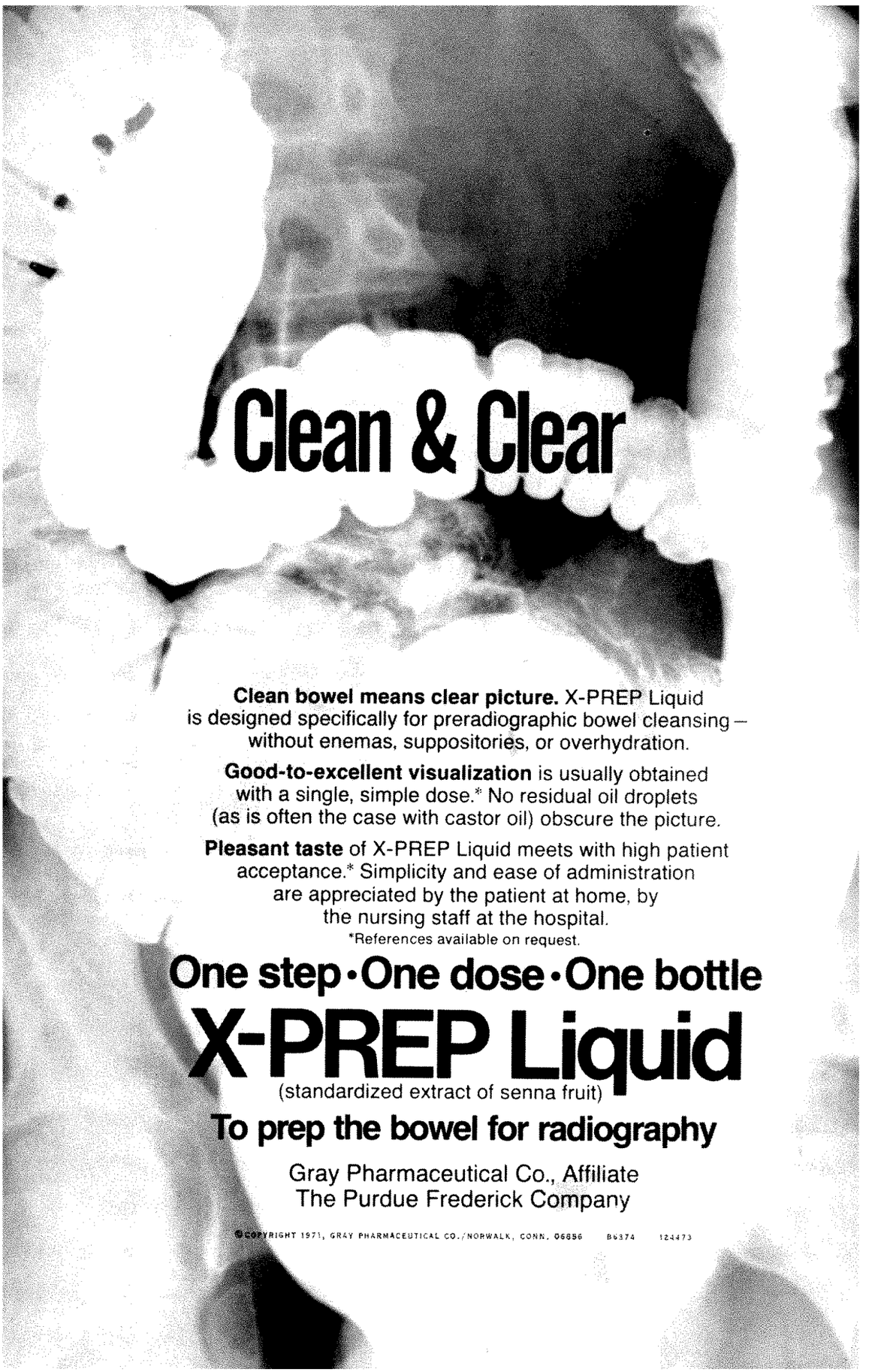
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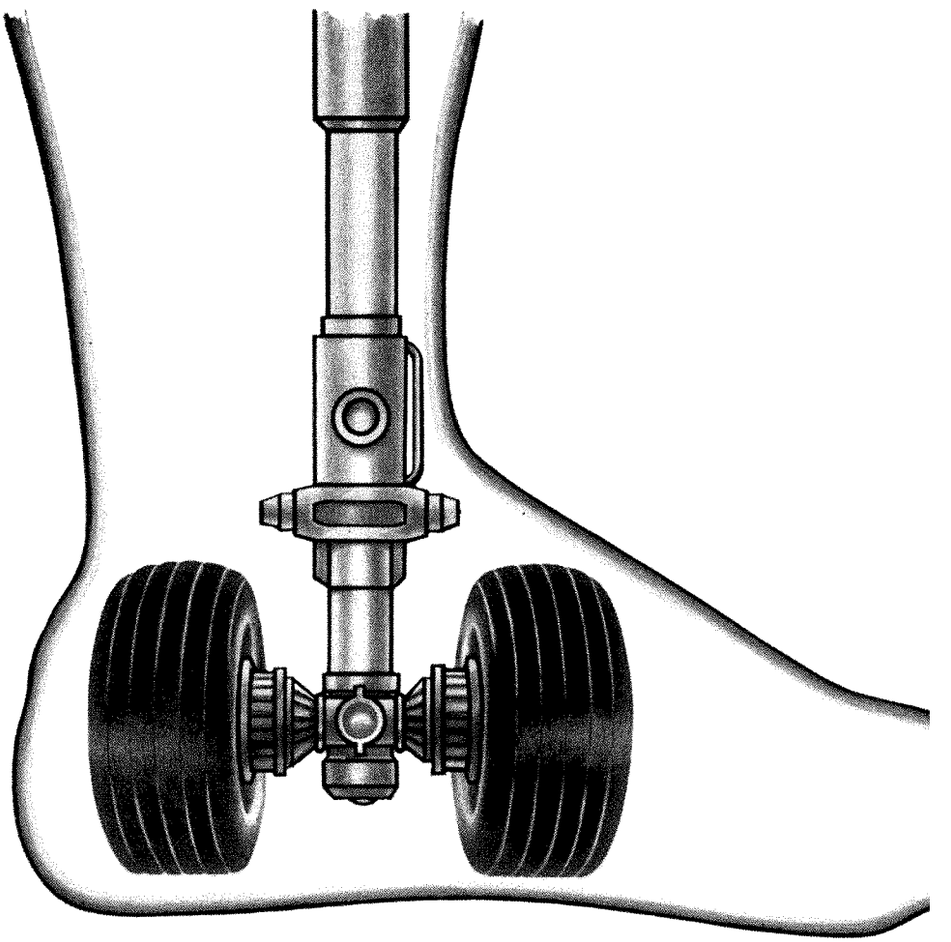
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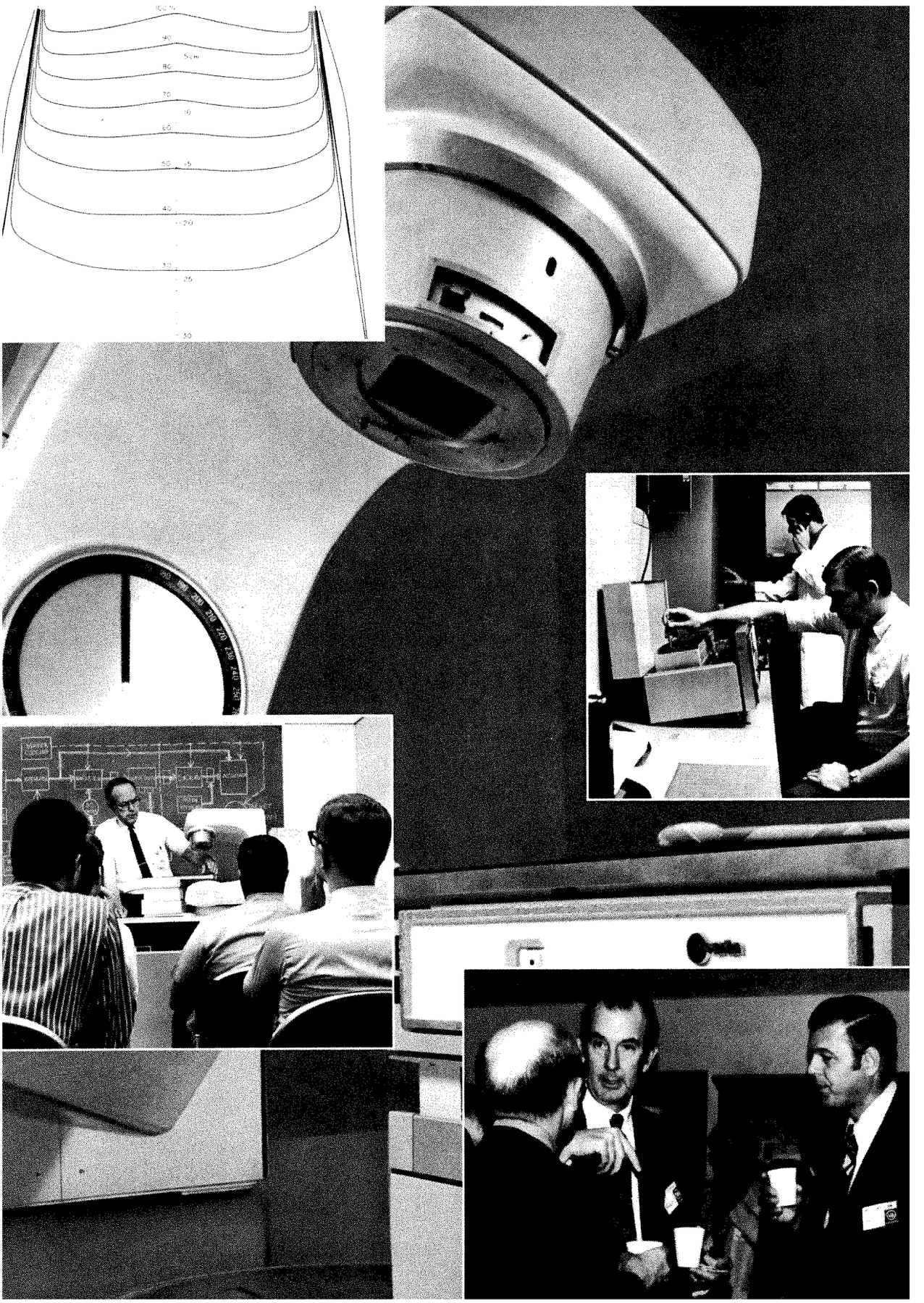
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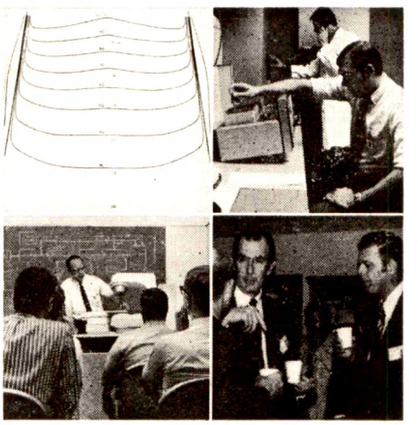
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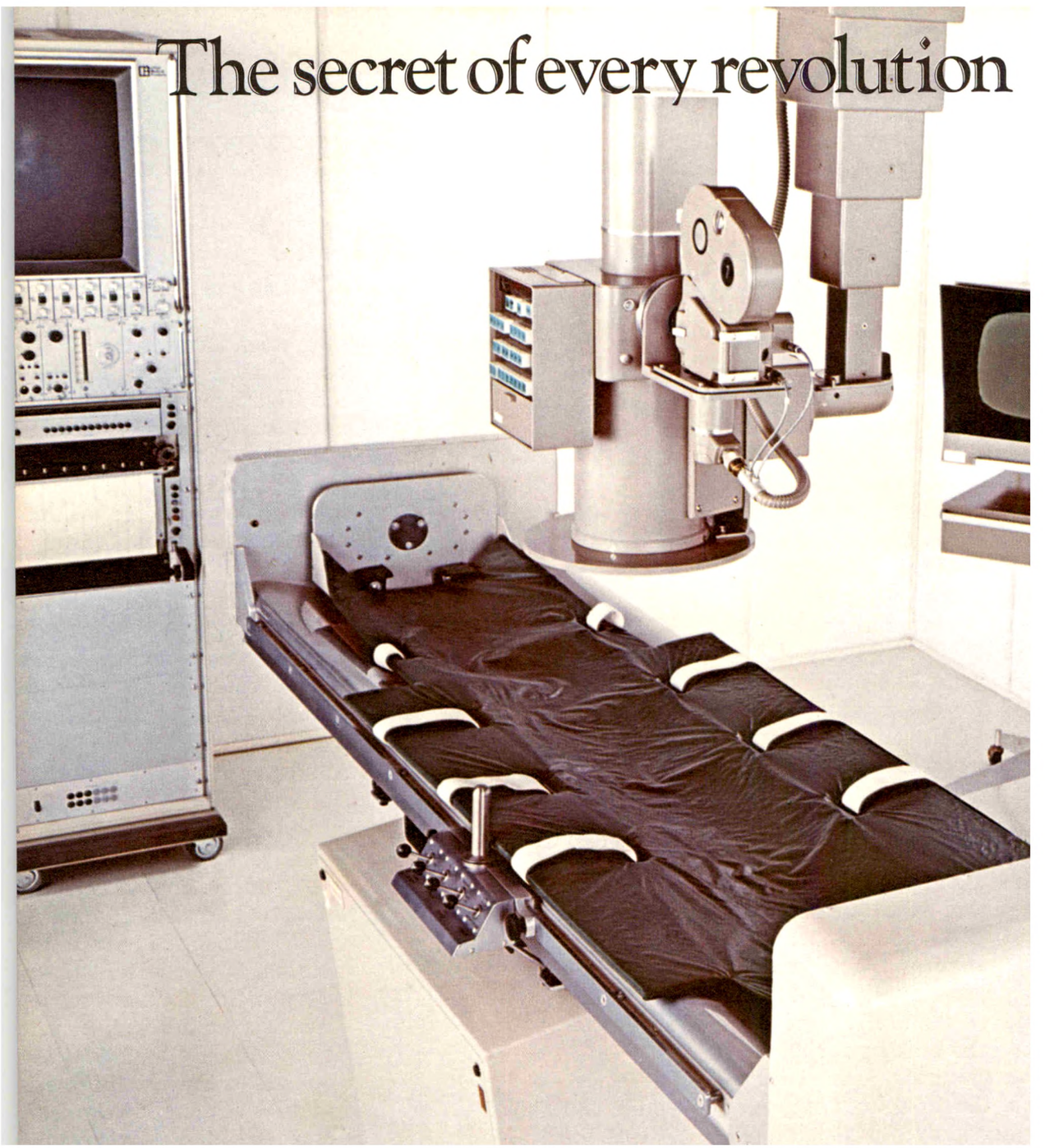
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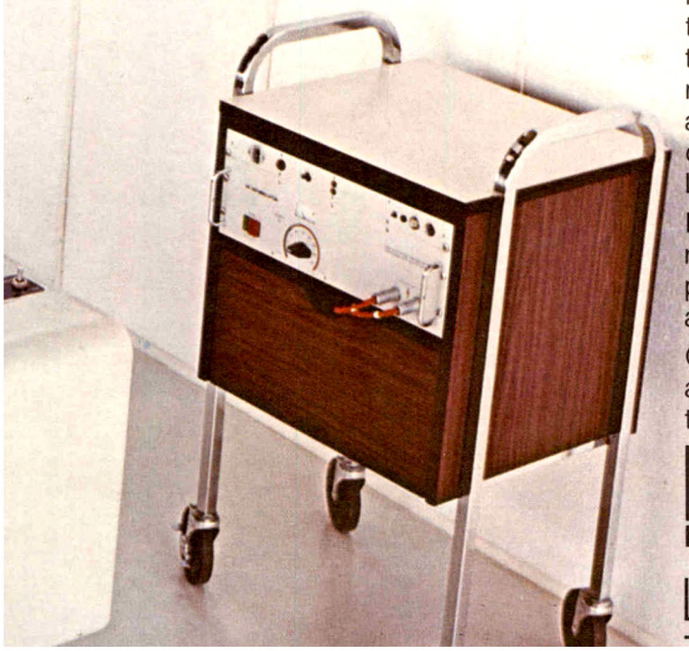
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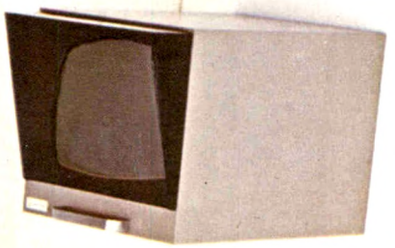
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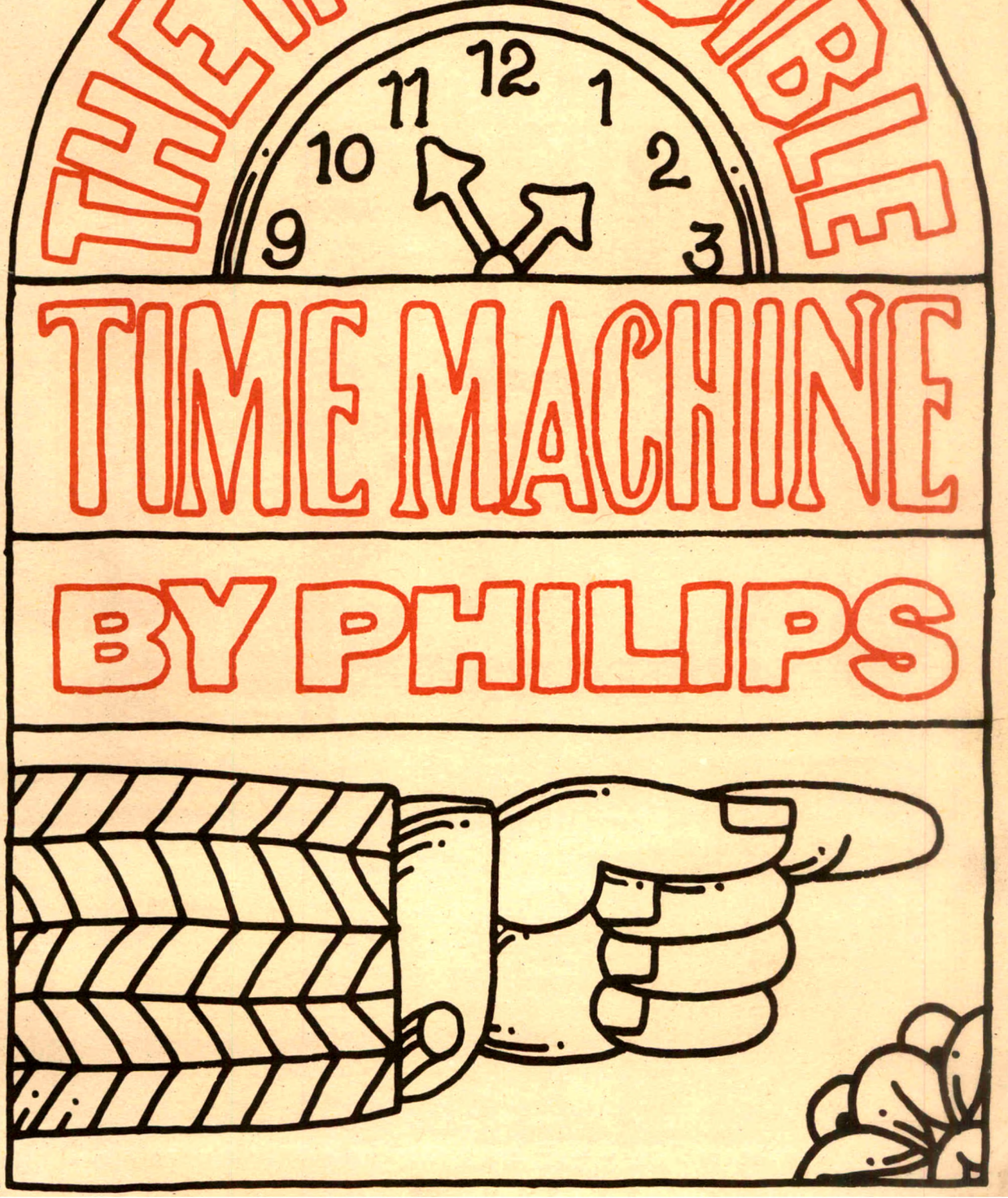
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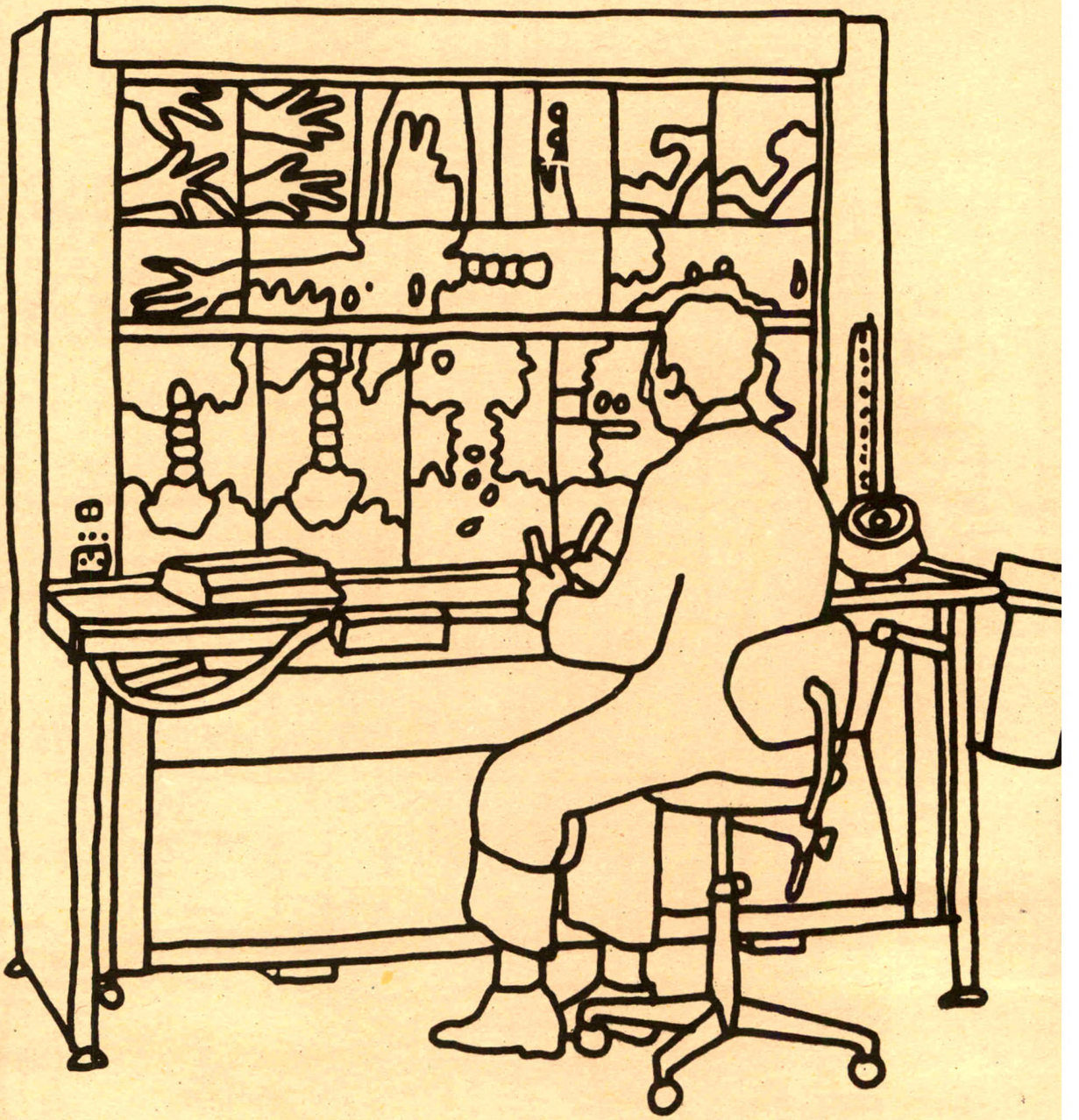
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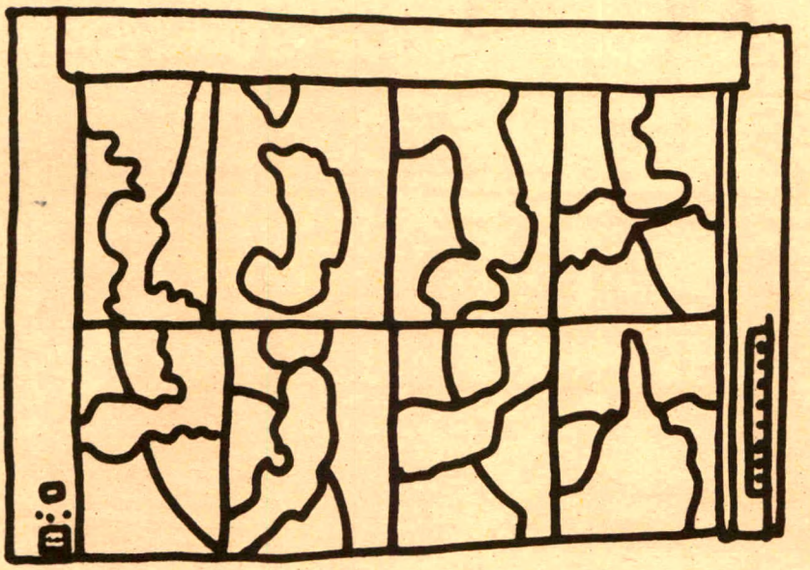


BY PHILIPS



1

We call this our Auto Alternator but it is really a time machine. Though it exists in three dimensions, it does some very interesting things with the fourth dimension: time. The most amazing thing it does to time is save it.
A lot of it!



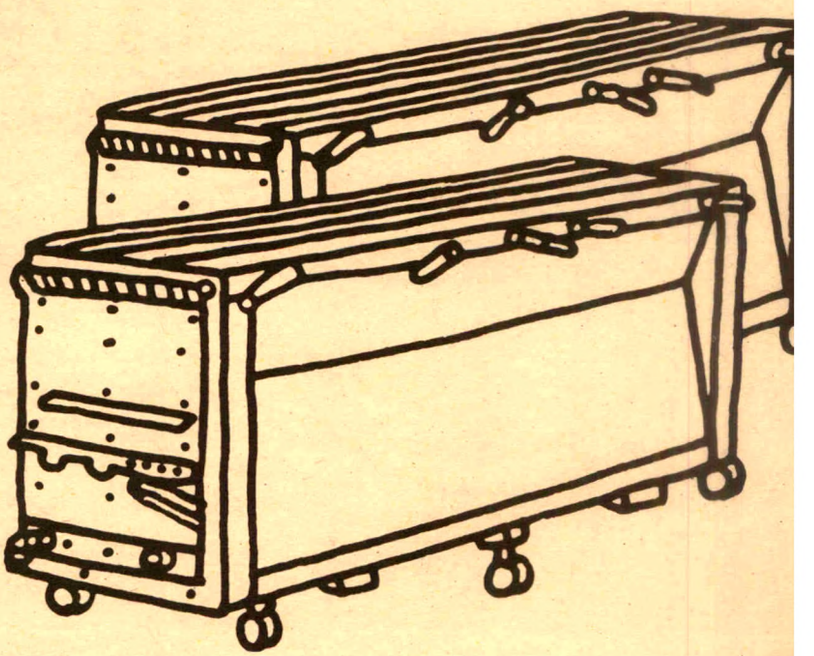
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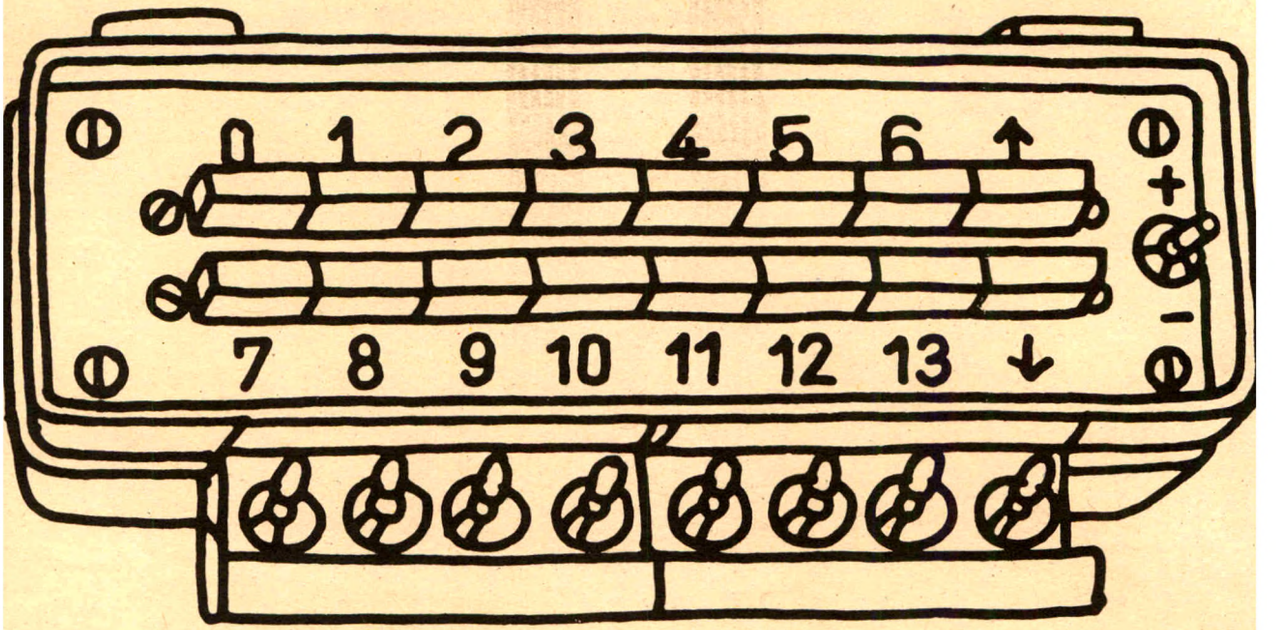
This is the viewing screen of the Auto Alternator. It illuminates eight 14 x 17 films in as little as 7 second after you call for them. These are selected from over a hundred stored in a magazine. The screen is divided into eight sections —each with its own light bank—and only the section behind the radiographs need be illuminated. Of course, the lighted section automatically dim while frames are changing.

3

This is the magazine trolley.

It is easily loaded with films and wheeled into the viewing room where it slides quickly into place in the Auto Alternator. Over a hundred films are ready to be read without waiting for one-at-a-time loading and unloading. Just one spare magazine will provide this fast changeover.

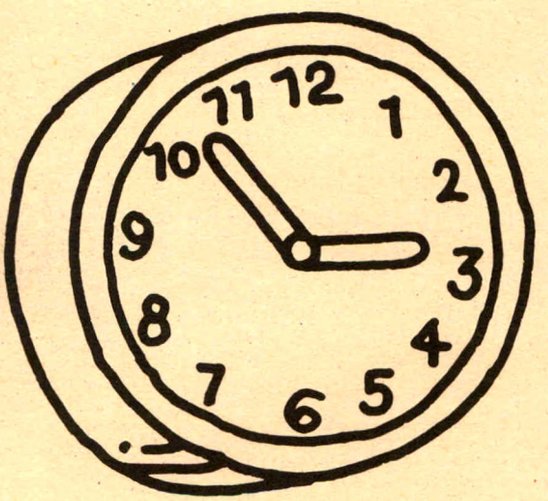




4

This is the switchbox.
It has buttons to move the films and switches to control the lights. Pushing any button returns a pair of frames to the magazine and brings up another pair with eight new films to view.
All this in just seconds!

5

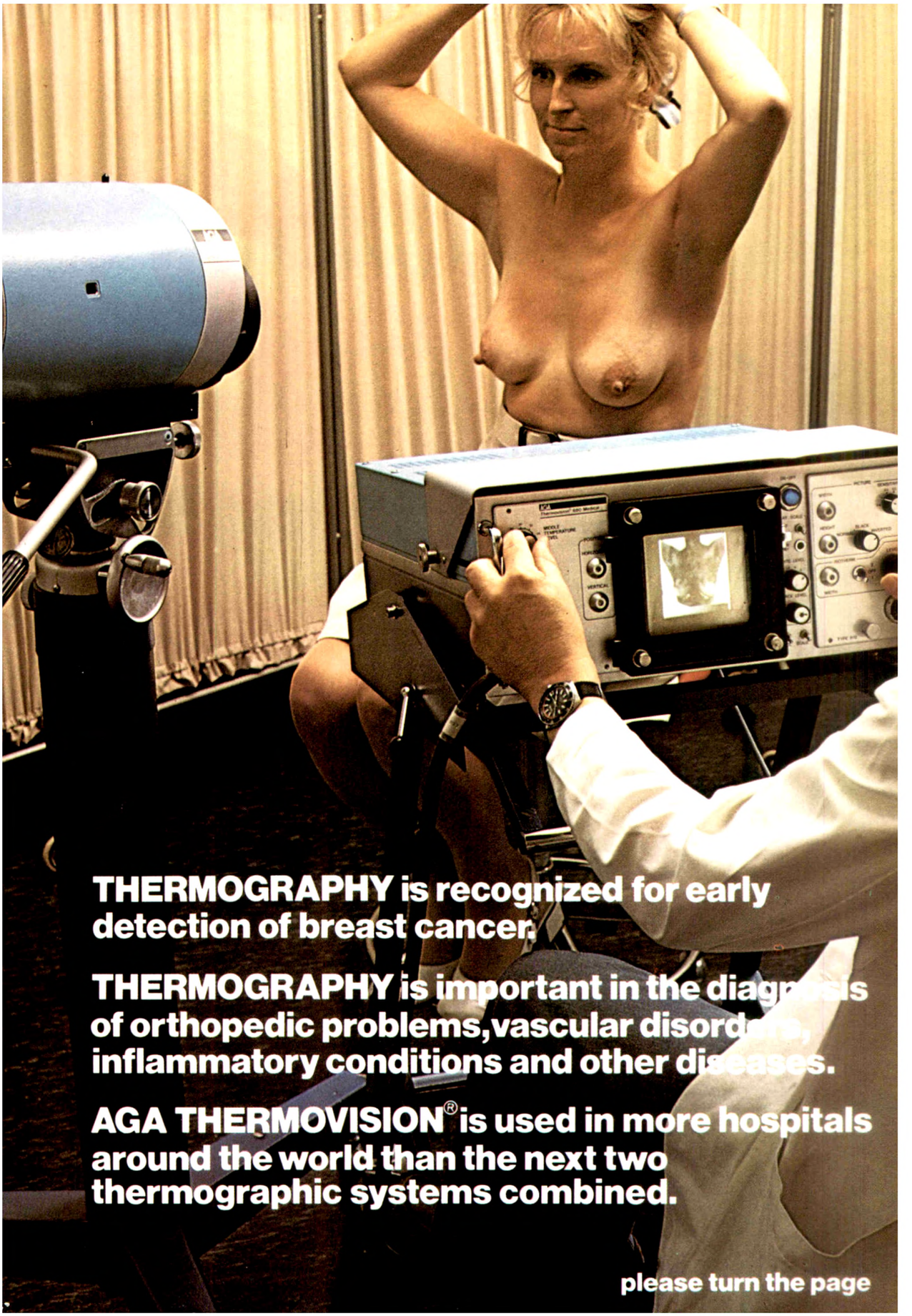


A strange thing happens to your clock when you use an Auto Alternator. There seem to be about twenty minutes more in every hour. Which means more films can be read every hour. All because films don't have to be removed from envelopes, **or** put up, **or** taken down **or** replaced into envelopes by the radiologist.

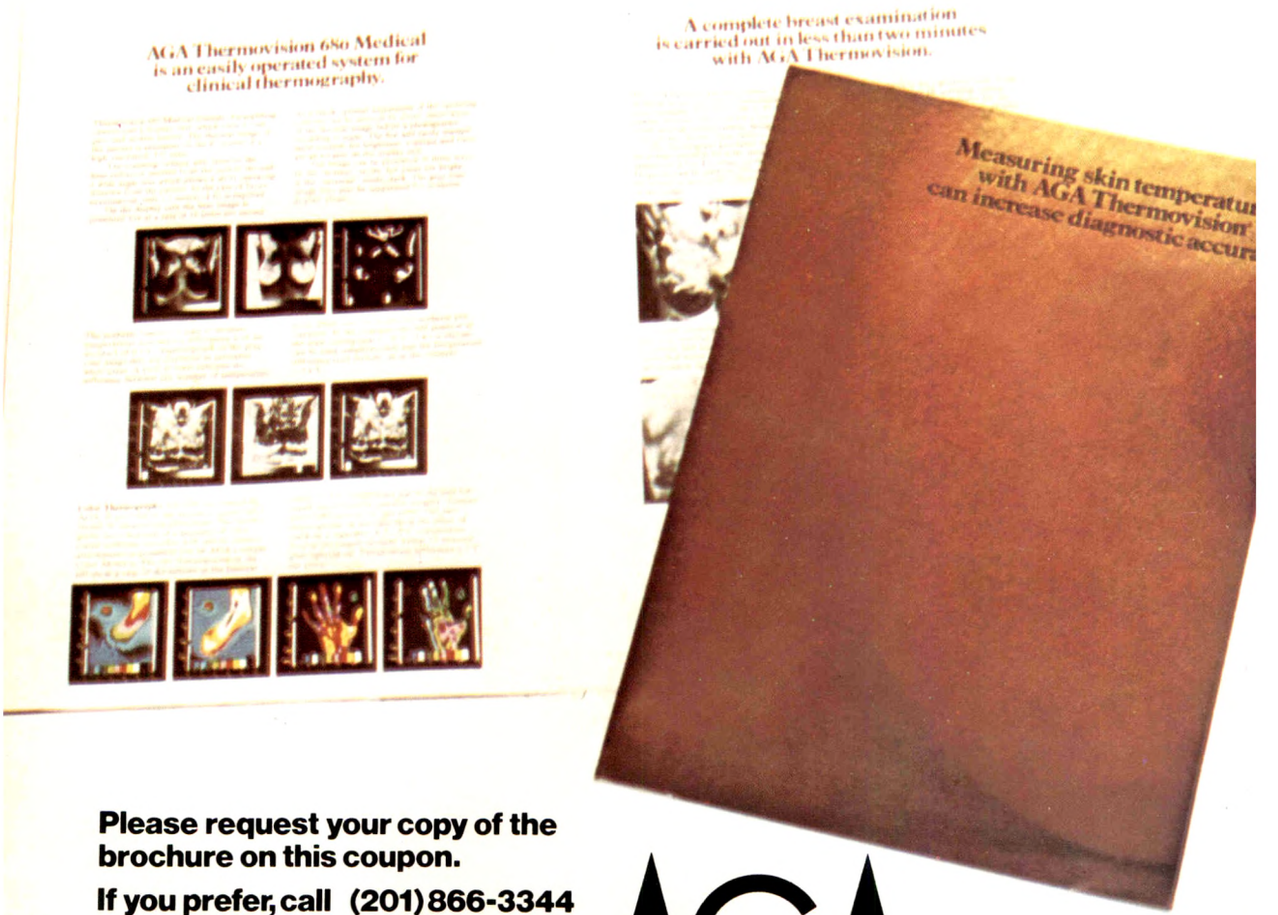
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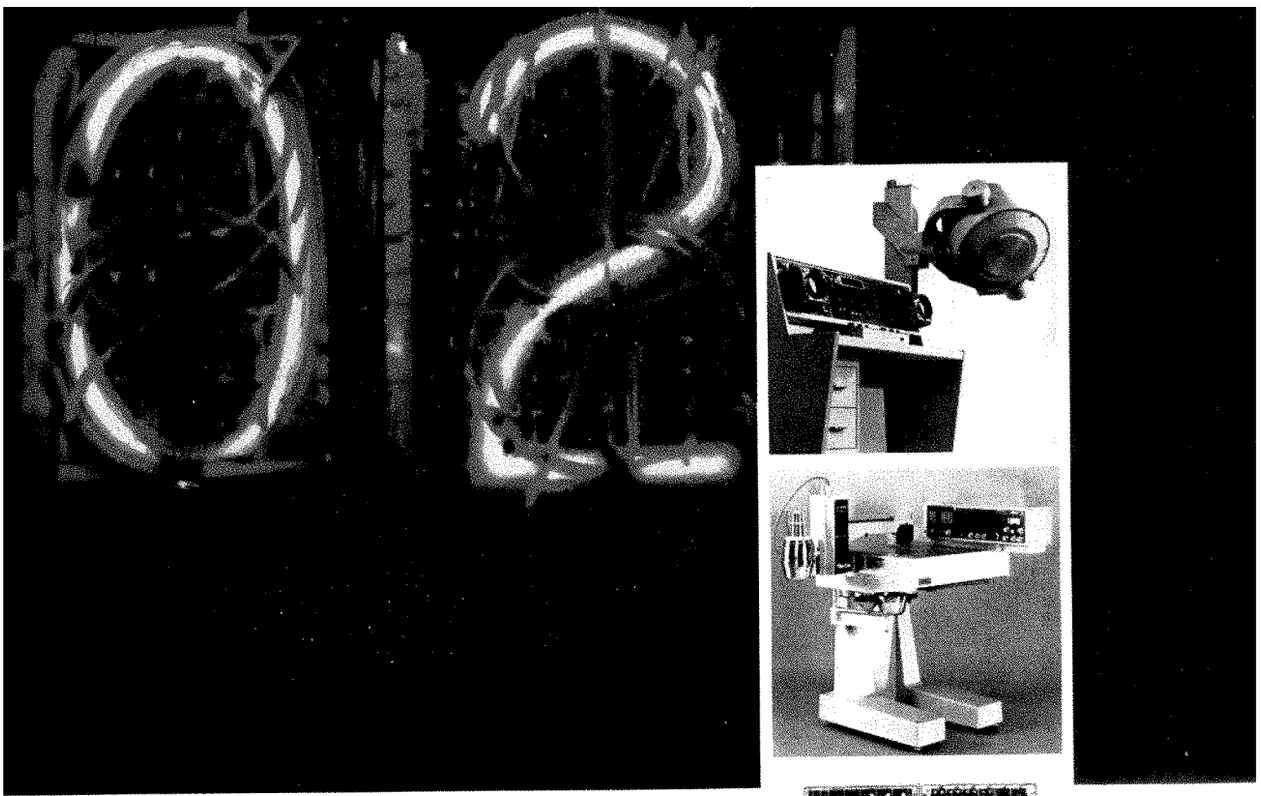
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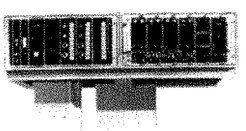
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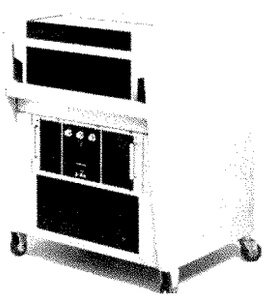
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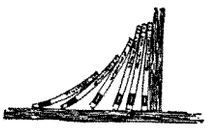
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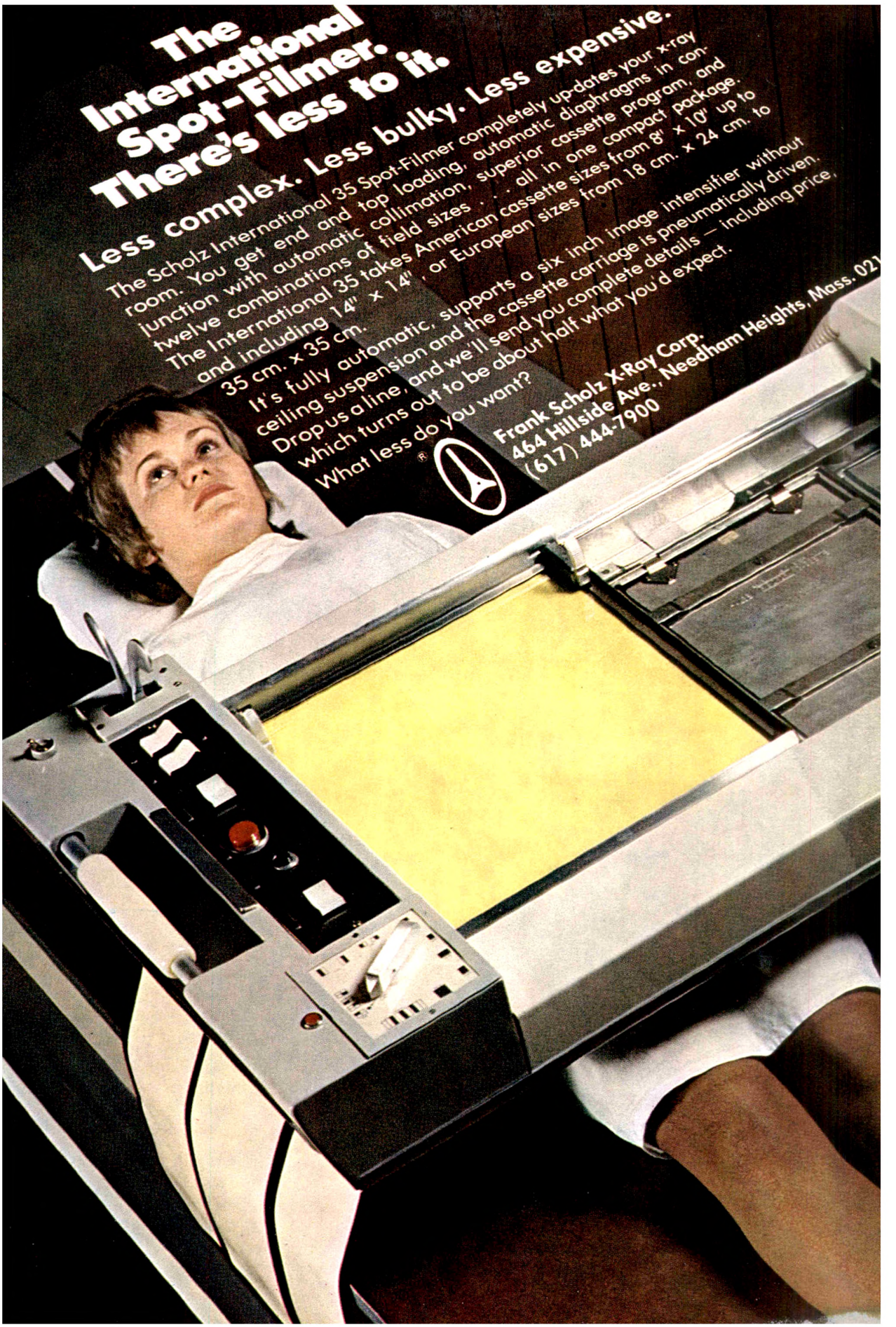
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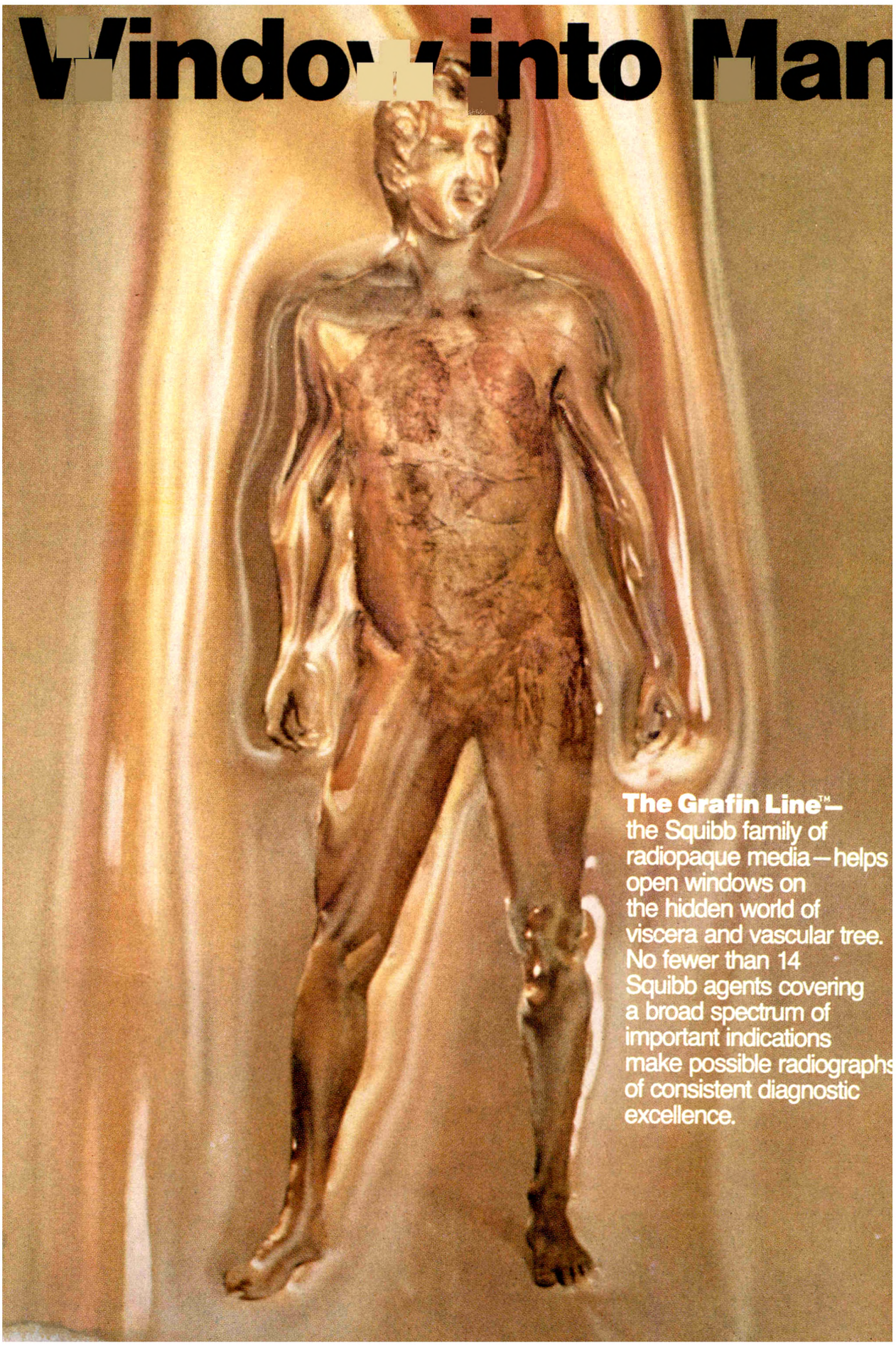
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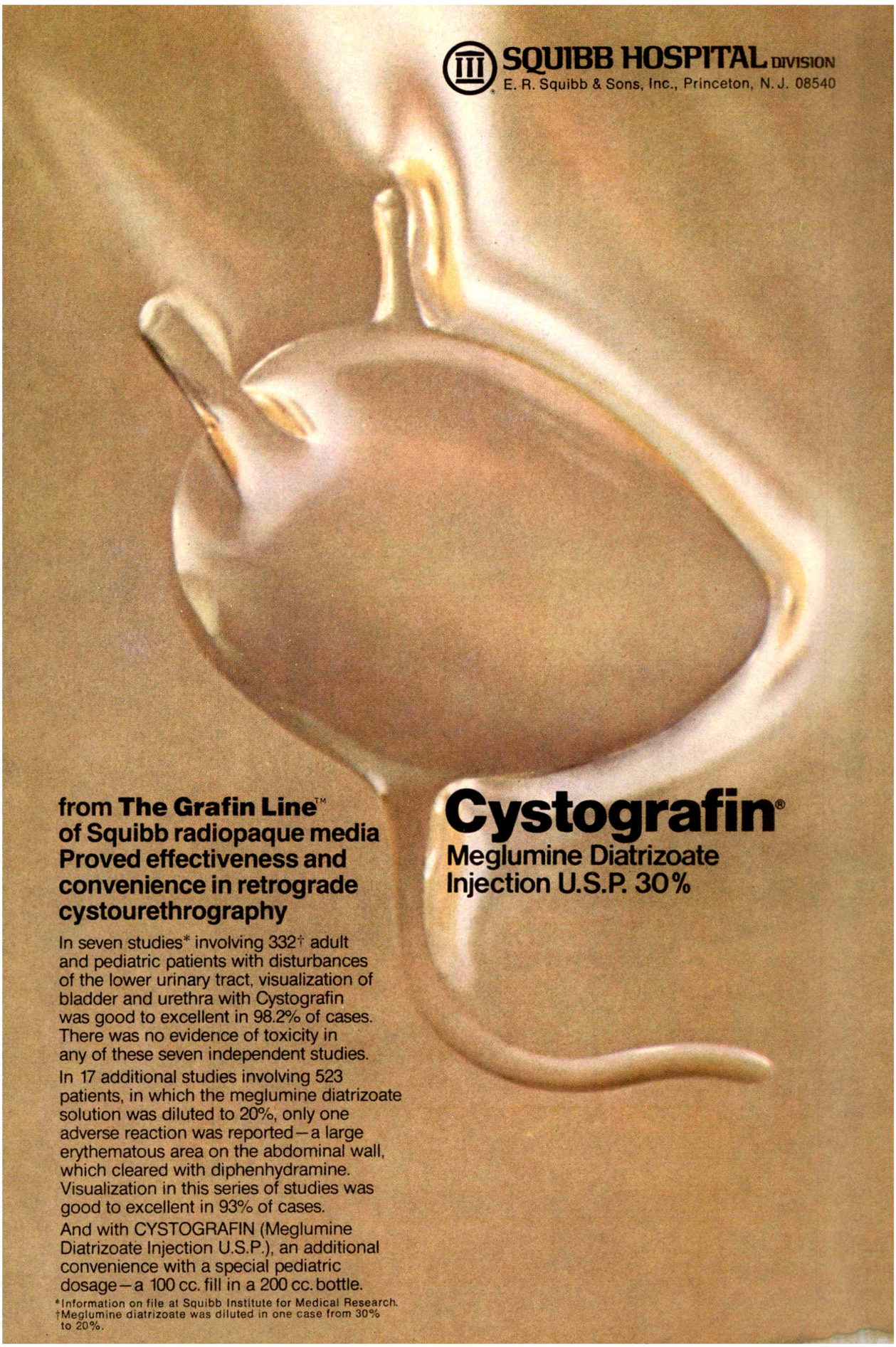
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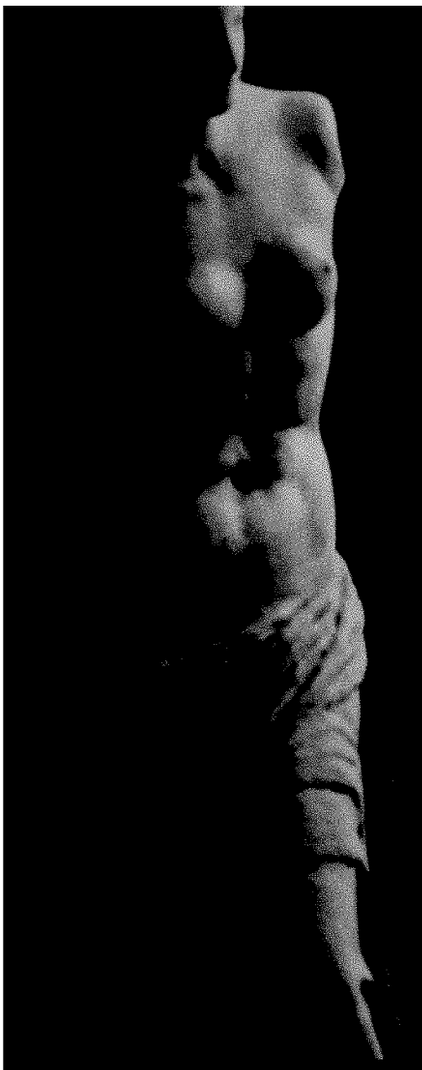
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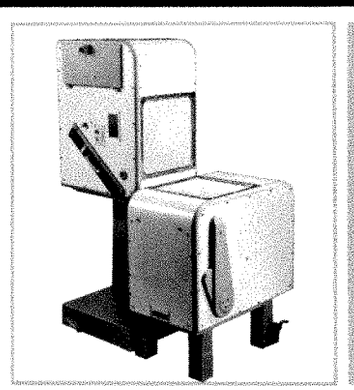
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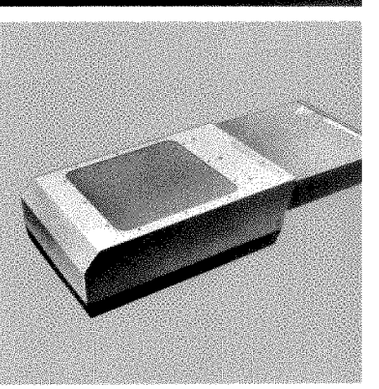
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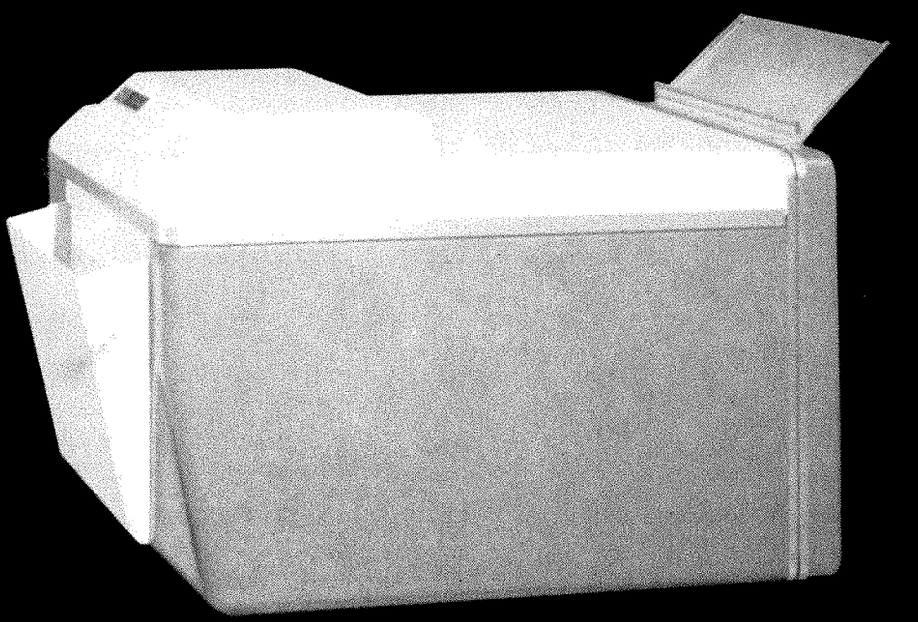
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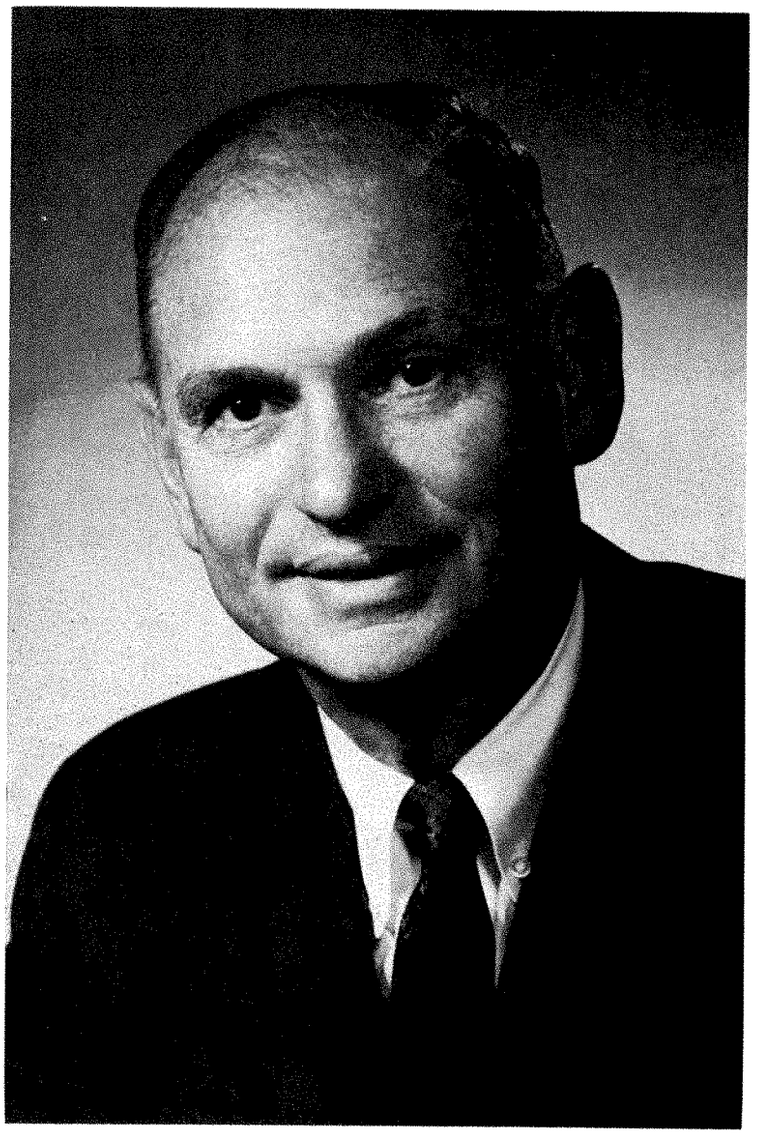
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ALEXANDER R. MARGULIS, M.D.
CALDWELL LECTURER, 1972

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INTRODUCTION OF THE CALDWELL LECTURER, 1972

By LEO G. RIGLER, M.D.
LOS ANGELES, CALIFORNIA

I am most grateful to President Dunbar for his kind words, but especially for the opportunity he has given me to introduce a former student, associate, colleague, and a dear friend, whose career has given me such pride and joy.

As I have left behind me the Biblical three score and ten, I have begun to add up the ledger, the debits and credits of a long life, to compute the legacy I would hope to leave behind; Dr. Alexander Margulis is one of those very special legacies. As the Caldwell Lecturer at this meeting, he exemplifies to a superlative degree the virtues for which Eugene Caldwell stood, the old verities of our generations. For he overcame many adversities by dint of industry, depth of character, complete dedication, and a superior intelligence to become one of the most distinguished of America's radiologists.

The wave of antihumanity, the holocaust which swept Europe in the 1930s and 1940s of this century, produced unexpected benefits for us in the United States. Driven out by their oppressors, many of their most talented scientists found their way to our shores to enrich our treasury of learning. Alexander Margulis came of a distinguished family in Yugoslavia—his father an eminent physician. Destined for medicine, he began his studies in Belgrade before the outbreak of the war, but then came the years which were horrible nightmares of fighting and oppression in Yugoslavia. Despite enormous difficulties, he finally made his way to the United States and in characteristically determined fashion began medical school all over again—if he were to be an American he would do everything possible to be a complete American, with a good American education. After graduation from Harvard University with many honors he took his radiology residency at the University of Michigan under Fred J. Hodges, where he at once established himself as a resident of unusual quality. Fortunately for us, he came to Minnesota just at the end of his residency, to nurture and enlarge upon his excellent background, making in a very short time a remarkable record. Never before had I seen anyone with such indefatigable energy, such initiative, such a profusion of new ideas and, in addition, such a cooperative, gracious personality. He collaborated so successfully with our colleagues that he came to be known as "the galloping ghost," carrying on his clinical assignments, while simultaneously doing a series of investigations with surgeons, internists, pediatricians and, of course, with other radiologists. In the short period of 3 years he took part in the produc-

tion of a book and some 21 papers, many of which broke new ground in roentgen diagnosis.

I take pride and satisfaction in the knowledge that I had some part in bringing him to the University of California San Francisco, where he has contributed so much to the medical school, to radiology, and to medicine, while achieving the distinction of his present position as Chairman of the Department of Radiology, and as wise counsellor to the University. He has developed a distinguished department, for he is one of those people who "violates natural law by being both the enzyme and the substrate in a working unit." With infinite patience he can criticize without offending. Beloved by his students and associates he exemplifies those qualities which make the true physician: "the art of caring about the patient, the art of transmitting his knowledge to his students, the art of making admiring friends of his colleagues."

Dr. Margulis has contributed extensively to the radiological literature and thereby has come to be an authority in the field of gastrointestinal diagnosis. His treatise with Burhenne is the definitive book on the radiology of the gastrointestinal tract. In addition, he has become one of the statesmen of radiology, Chairman of the Association of University Radiologists, Chairman of the Society of Chairmen of Radiology Departments, and he has been honored on numerous other occasions which I need not relate here. I will say that in 1970 he became one of the two living Americans who are Honorary Fellows of the British Faculty of Radiologists. Indeed his relations with our colleagues abroad has brought honor and distinction to our own radiological community.

You may recall that when Alexander the Great asked Diogenes if he could help in any way, the answer was: "Only stand out of my light." Our own Alexander has learned to stand out of the light of his gifted students and colleagues; so that they in turn may become leaders of radiology in the United States.

Amongst the many distinguished Caldwell lecturers of the past, I am certain that Eugene Caldwell would appreciate none more than Dr. Alexander Margulis, who will address us on "The Lessons of Radiobiology for Diagnostic Radiology."

Vol. 117, No. 4

THE LESSONS OF RADIOBIOLOGY FOR DIAGNOSTIC RADIOLOGY*

CALDWELL LECTURE, 1972

By ALEXANDER R. MARGULIS, M.D.
SAN FRANCISCO, CALIFORNIA

IN this era of great consciousness about ecologic matters and environmental hazards, it is not surprising that a great deal of attention is being paid to the effects of diagnostic radiology on human populations. That radiation can be damaging is not a new discovery and radiation protection is not a fad. Effects of diagnostic radiation on patients, on their offspring, and on radiologists have been studied since 1896.

While diagnostic roentgenology has undoubtedly been tremendously valuable in the progress of medicine in this century, it is important for diagnostic roentgenologists to be aware of the potential damage that their usually valuable contribution to the welfare of the patient is capable of inflicting. To understand the problem, to arrive at useful and rational recommendations and solutions, it is necessary to examine the accumulated evidence about the damage as well as the benefits of diagnostic radiation. It is important to do so without joining a parade of hysterical concern that has almost religious overtones and dismantles useful structures because they are not without risk.

Before presenting the evidence about damage from radiation in the diagnostic range and some evaluation of the good emanating from our specialty, I should present my credentials for discussing this subject.

First, I am not known to be an expert in the fields of radiobiology and radiation protection, which means that I have no previous stands to defend, and I hope you will believe that I have no previous prejudices. My second point of eligibility for talking about this subject is that, as a gastrointestinal radiologist, I have been not only one of the major dispensers of diagnostic radiation energy to patients, but also, among radiologists, one of the major consumers of this energy.

HISTORICAL REVIEW

Almost from the moment of Wilhelm Conrad Röntgen's discovery of x rays on November 8, 1895, the great advantages of their application to diagnosis were offset by harmful effects. For a long time diagnostic radiation was used with abandon and almost no protection for the radiologist, the auxiliary personnel, or the patient. Almost all of the clinical diagnostic roentgenologists in this early era suffered some type of injury to their hands. Many lost their fingers or developed multiple cancers of the skin and other organs, and a number succumbed to leukemia. Viewing photographs of how early fluoroscopy was performed and how plates were exposed, one can readily understand why clinically obvious damage occurred frequently.[18]

Nearly 1,000 publications and several textbooks on x rays appeared within the first year after the announcement of Roentgen's discovery.[34] In some of them diagnostic radiologists reported on radiation damage, but they were not aware of the insidious delayed damage radiation caused both to themselves and to their patients.

Concerned workers in the field of radiation protection recommended precautionary measures to reduce the hazards as early as 1916.[7,43] The general public, however, did not become aware of the potential

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
From the Department of Radiology and Laboratory of Radiobiology, University of California, San Francisco, California.
Work performed under the auspices of the U. S. Atomic Energy Commission.

TABLE I

CHANGES IN RADIATION PROTECTION STANDARDS FOR THE RADIATION WORKER*

Recommended Rate†	Comments
0.2 r/day (or 1 r/wk.)†	Recommended as a tolerance exposure by ICRP in 1934 and continued in worldwide use until 1950.
0.1 r/day (or 0.5 r/wk.)‡	Recommended as a tolerance exposure by NCRP on March 17, 1934, and continued in use in the U.S. until 1949.
15 rem/yr. (0.3 rem/wk.)	Recommended as a maximum permissible dose by NCRP on March 7, 1949, and ICRP in July 1950; continued in use until 1956.
5 rem/yr. (0.1 rem/wk.)	Recommended as a maximum permissible dose by ICRP in April 1956 and NCRP on January 8, 1957.

* Courtesy of K. Z. Morgan[33] and Radiation Research Society.
† The values are in addition to medical and background exposure.
‡ Based on a 5 day work week.

dangers of radiation until after the atomic bombing of Hiroshima and Nagasaki in 1945 and the subsequent testing of atomic fission and fusion bombs in the atmosphere. The scientific community began to publicize its warnings after 1945 in order to inform the public about the general population risk from medical radiation as well as the individual risk for patients and their offspring. Besides constructive suggestions in scholarly journals by experts in radiation protection, articles also appeared in the *Ladies' Home Journal*,[35] *Reader's Digest*,[58] and *Consumer Reports*.[60]

Although radiologists have recommended radiation protection measures since 1916, there has been a great deal of delay in enacting them. In 1934 the International Commission on Radiation Protection (ICRP) adopted the concept of a tolerance dose and recommended that the rate should not exceed 0.2 rad/day for radiologists and their personnel. The concept of tolerance dose has since been replaced by that of maximum permissible dose,[51] in recognition of the fact that there is no tolerance to radiation, but only an acceptable risk for workers in the radiation field. The present maximum permissible dose for workers is 5 rem/year to the most critical body organs (active bone marrow, gonads, and the total body) (Table 1).

The dose that the population gets from medical exposure should be kept to a minimum. This dose is not insignificant at present. A 1968 study pointed to a genetically significant dose of 50 mrad from diagnostic radiology in New York City.[36] A similar genetically significant dose was estimated for the United States population in 1964 and it was suggested that this could be reduced to 19 mrad if collimation were used to limit beam size to film size in the plane of the film.[37]

In August 1972 the Bureau of Radiological Health of the FDA decreed that all manufacturers must produce diagnostic x-ray equipment capable of restricting the beam to the size of the x-ray film used or the fluoroscopic receptor. This is an important step which will significantly reduce the amount of radiation to patients and radiologists. The equipment will also have to incorporate features that will make it possible for the operator to obtain a desired image quality at given machine settings for voltage, current, and time more consistently than he can at present.

Let us now examine some of the reasons for this concern about seemingly very low doses of radiation.

SOMATIC EFFECTS OF TOTAL BODY IRRADIATION

A large fund of data exists on the somatic effects of ionizing radiations. They are derived from a huge body of experimental work in animals, as well as from human data. Among the latter, material emanating from studies of the Atomic Bomb Casualty Commission is the most extensive and informative. Many epidemiologic studies are also available, assessing the effects on both patients and operators subjected to this radiant energy.

Somatic effects may not be expressed for years or even decades after irradiation. Thus far, most studies do not exceed 25 years. The observations have to be based on excessive occurrence of diseases in the irradiated population which also afflict non-irradiated human populations. Epidemiologic deductions thus become statistical and are difficult to interpret accurately since over the decades, many other influences come into play, confusing the effects of radiation alone.

A great deal more is known about the effects of radiation in large doses and at high dose rates than at low-level exposures for both animal and human populations. One would expect that experimental data obtained under controlled conditions would provide clearer answers about effects of low dose levels and rates, but unfortunately our understanding of the sequelae of doses smaller than 50 rem is far from complete. In this area of great importance, it is not yet clear whether radiation effects are to be extrapolated to the lowest dose as a linear or curvilinear function. If curvilinear, is the curve convex or concave, and is there a threshold?

The curves in Figure 1 illustrate the difficulties in interpretation and extrapolation. The evidence is simply not available yet for the effects of doses in the low range.

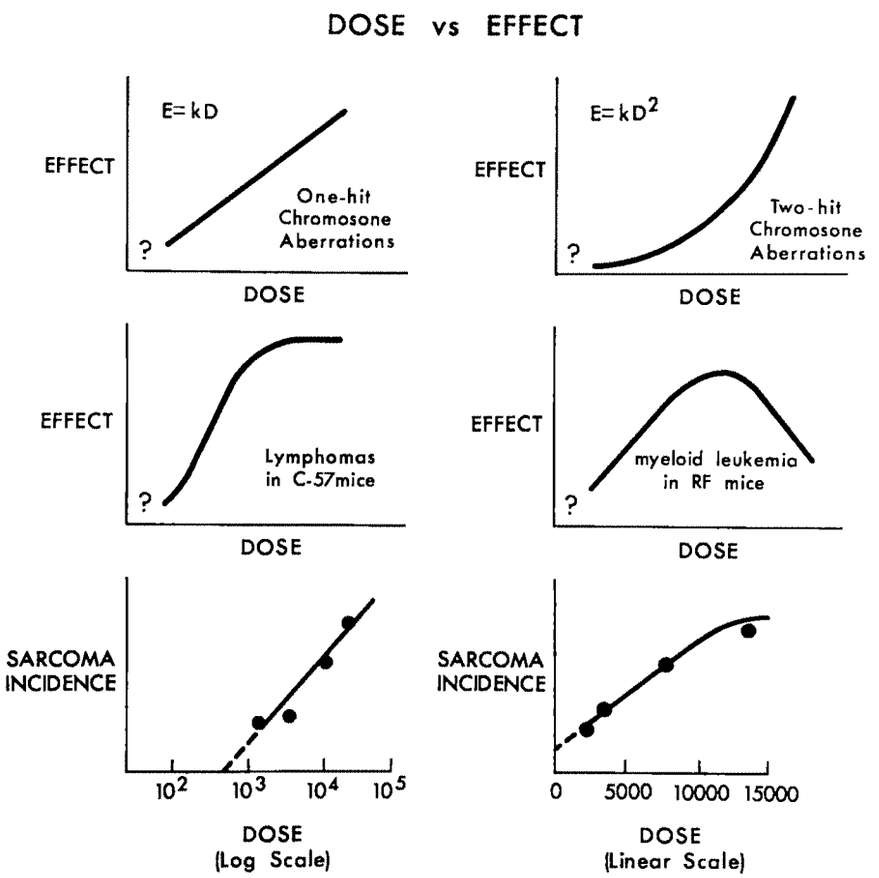


Fig. 1. Radiation dose *vs.* biologic effect curves. The dose scale of the two sarcoma-incidence curves is marked (based on data from Rowland *et al.*[42]). The dose range of the curves for incidence of lymphomas in C-57 mice (from Kaplan and Brown[22]) and myeloid leukemia in RF mice (from Upton *et al.*[53]) is from 0 to 600 rad. The sarcoma curves show the incidence of bone sarcomas from various levels of accumulated dose from body burdens of radium. In all curves there is a lack of information at the lowest dose levels.

The one-hit chromosome aberration curve is linear, the two-hit curve is concave. The data on lymphomas fit into a slightly convex curve.[22] The curve by Upton and his co-workers for the incidence of myeloid leukemia in RF mice after radiation is linear to about 150 rad, at which point its slope decreases to approximately 300 rad and then assumes a downward direction.[53] Yet in all these curves of varied shapes the take-off from the baseline is missing. The method of plotting data can also create confusion. The curves indicating incidence of bone sarcomas due to various levels of accumulated dose from body burdens of radium, as obtained by Rowland *et al.*,[42] are either straight or curvilinear, depending on whether the dose is plotted on a logarithmic or a linear scale. The data are the same, but the direction of the curve and its intersection with the baseline is left to the imagination of the interpreter.[42] Although there is some evidence that the effect-dose curve for low dose rates of x irradiation and gamma irradiation may be concave, the proof is not beyond question.[44]

For the purposes of safety we must accept the risk of erring on the conservative side. Hence, most advisory committees base their recommendations on the assumption of a linear hypothesis in order to protect the public in an area of potential danger where all the data are not yet available. When making precise calculations on the exact number of deaths caused by diagnostic radiation as some scientists have been doing, it is important to protect the public from alarm and anxiety by pointing out that the conclusions are based on assumptions and are, in effect, as yet unprovable.[15,33]

The main somatic effects of radiation are production of leukemia, benign and malignant neoplasms, impaired fertility, cataracts of the lens, and non-specific effects such as shortening of life and ageing.

In the range of diagnostic radiation, only consideration of leukemia and neoplasms seems to be warranted. The production of other somatic effects appears to require considerably higher doses.

INDUCTION OF LEUKEMIA BY RADIATION

Upton *et al.*[53] have shown a 30 per cent incidence of myeloid leukemia in RF mice after irradiation at high dose rates and at doses of 200 to 300 rad of total body irradiation. The induction of leukemias was reduced at low dose rates.

More recently, Gong[16] has reported a 100 per cent incidence of leukemia after total body irradiation of Sprague-Dawley female rats, which were bled of approximately two-thirds of their blood volume a month or so later. All the rats exposed to total body irradiation doses of between 50 and 350 rad died of what appeared to be a myelogenous leukemia by 16 months after bleeding. Gong believes that bleeding served as a specific stress to the bone marrow, which had been rendered leukemia-prone by x irradiation. From his published curves, it is interesting that 50 rad was more effective than 350 rad in producing leukemia. Even unbled rats, in a strain normally not susceptible to myeloid leukemia, had a fairly high incidence of this disease after irradiation. The curve of incidence of leukemia starts around 25 rad and reaches its maximum about 200 rad, when approximately 45 per cent of the unbled, irradiated rats developed myelogenous leukemia.

Since patients who receive multiple diagnostic roentgen studies may conceivably receive doses of 25 rad to a large area of the body and since, conceivably, some of these patients might suffer severe hemorrhage from an unrelated cause, this work is alarming and has great potential significance for diagnostic radiology. It is for this reason that we attempted to duplicate Gong's work using larger groups of animals. There was, however, at least one obvious difference: our animals were caged singly in order to avoid infection. In the 6 months since the rats were bled, none have contracted leukemia and their blood and mar-

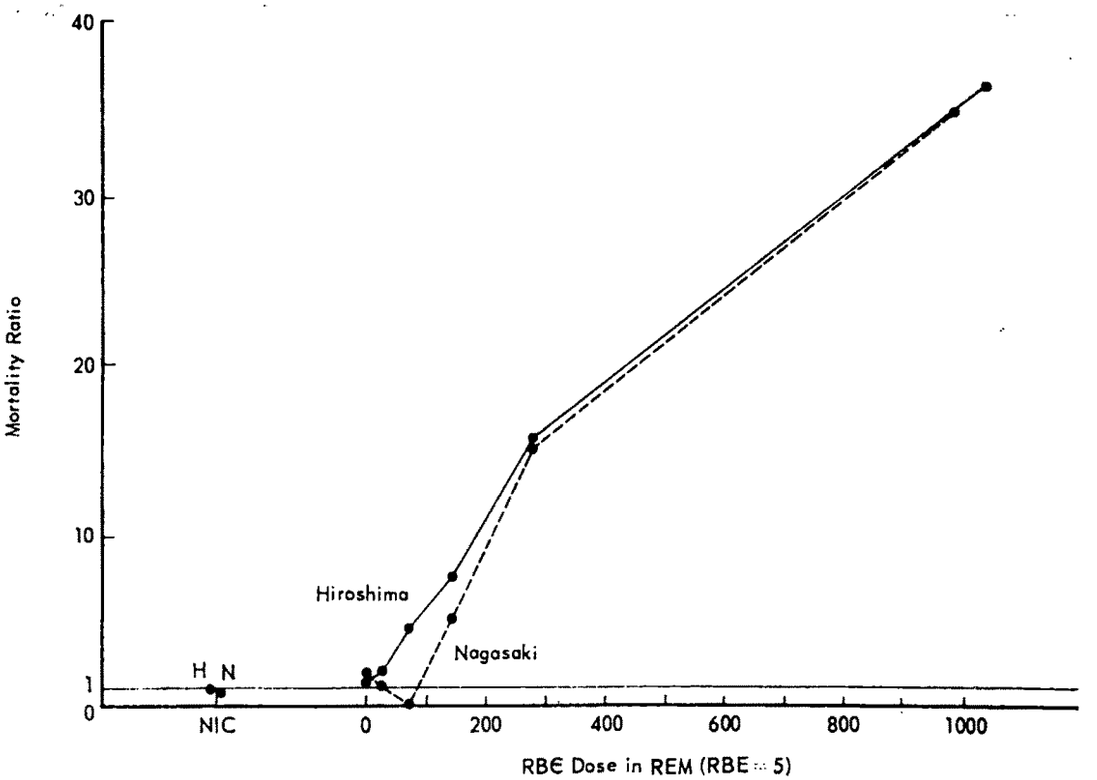


FIG. 2. Mortality ratios for leukemia. (Courtesy of S. Jablon and H. Kato,[21] and *Radiation Research*.)

row counts have remained normal. One rat was sacrificed after appearing ill. Grossly, the animal seemed to be suffering from leukemia; slides of the bone marrow, peripheral blood, and liver, as well as other organs, however, showed evidence of an overwhelming infection. Even hepatocytes showed evidence of damage and active proliferation as demonstrated by tritiated thymidine uptake. Significantly, perhaps, red cells in the peripheral blood showed *Bartonella* organisms.

Our failure thus far to reproduce Gong's results raises the question of whether his criteria for diagnosis of myelogenous leukemia were rigorous enough to exclude the possibility of a primary response to overwhelming infection (in effect, a leukemoid reaction).

The most exhaustive and the largest studies to date on the effects of radiation in the production of leukemia in man are those conducted by the Atomic Bomb Casualty Commission. The newer dosimetry (T-65) takes into consideration the fact that the Hiroshima bomb contained a large amount of its radiation energy in fast neutrons, while the radiation at Nagasaki was predominantly gamma. Neutrons, with their high linear energy transfer, are more effective in carcinogenesis. Using a relative biological effectiveness (RBE) of 5 for neutrons, leukemia curves for the 2 cities are rather similar (Fig. 2). Age was a factor in the susceptibility of atomic bomb victims to radiation. Children under the age of 10 had the highest risk for developing leukemia. This risk decreased between the ages of 10 and 19, then increased slowly after the age of 20, being fairly high in people over 50.[21]

The dose-effect curves are fairly easy to interpret on a linear basis from an exposure to approximately 100 rem, but the picture

at lower doses remains unclear. One must realize that the data were derived from truly cataclysmic explosions which were associated with high dose radiation. In addition to the radiation, however, there was a blast effect, the heat resulting in burns and great disruption of normal supplies of food and water to large cities, as well as loss of shelter. All of this complicates an exact interpretation of data. Nevertheless, this is the largest, best documented, and best analyzed study of radiation effects on human beings to date.

Interesting data have also been obtained on development of leukemia after diagnostic x-ray exposure during intrauterine life. Stewart and her associates have published a number of articles since 1956 based on a group of children who died of leukemia and other children free of cancer who were controls. Each mother was interviewed to obtain a history of irradiation during pregnancy. An almost two-fold excess of leukemia over the controls was encountered in the children who had had intrauterine radiation.[48–50] Using obstetric records in a number of maternity hospitals in New England for the period 1947–1954, MacMahon examined the frequency of diagnostic radiologic examinations of pregnant women whose children died of cancer and compared this with controls obtained by a sample of 1 per cent of other births in the same hospital. His results also showed a 40 per cent increase in the likelihood of leukemia in children exposed to radiation *in utero*.[29] In a prospective study of 20,000 children exposed to diagnostic radiation *in utero* and 40,000 controls, Diamond and Lilienfeld[10] found that 6 white children developed leukemia, although only 2 such cases were expected. No leukemia occurred in *in-utero*-exposed black children.

Induction of Cancers Other Than Leukemia by Radiation

The kinds of tumors other than leukemia that can be experimentally produced in animals are too numerous to list. Almost no organ is spared. There is no question that radiation is potentially carcinogenic to nearly all tissues under the proper conditions.[52] For example, mammary tumors have been induced in mice[55] and rats.[47] Thus, the results of a study on Sprague-Dawley female rats indicate that the incidence of mammary tumors induced by radiation is linearly related to dose in the range from 25 to 400 rad.[6]

That total body irradiation can produce cancers other than leukemia in man has also been reported in several studies by the Atomic Bomb Casualty Commission. Their data indicate that the latent period for cancers other than leukemia is longer than the latent period for leukemia (Fig. 3). Thus, the leukemia incidence in atomic bomb survivors was higher than that of other cancers up until 1960; it then started to decrease while the incidence of other cancers began to rise, increasing significantly between 1965 and 1970.[21]

The curves plotting dose against mortality ratios (the number of deaths observed compared to expected deaths at Japanese national rates) show a relative linearity from 200 rem up (an RBE value of 5 being assigned to the Hiroshima calculations); the curves of Hiroshima and Nagasaki survivors are fairly similar. However, the curve below 200 rem for the Nagasaki survivors is well below the Hiroshima curve (Fig. 4). The reason for this discrepancy is not yet understood.

The epidemiologic studies of Stewart and her associates and those of MacMahon revealed an increased risk of cancers other than leukemia among children irradiated *in utero*. Stewart and Kneale came to the conclusion that the crude excess cancer risk was directly proportional to the number of diagnostic x-ray films of the pregnant mothers.[49] MacMahon demonstrated an approximately 50 per cent increase of all cancers in children exposed to radiation *in utero*.[29] In their prospective study, Diamond and Lilienfeld showed no excess of cancers other than leukemia in either white or black children.[10] Although Stewart and Kneale showed that many types of cancers

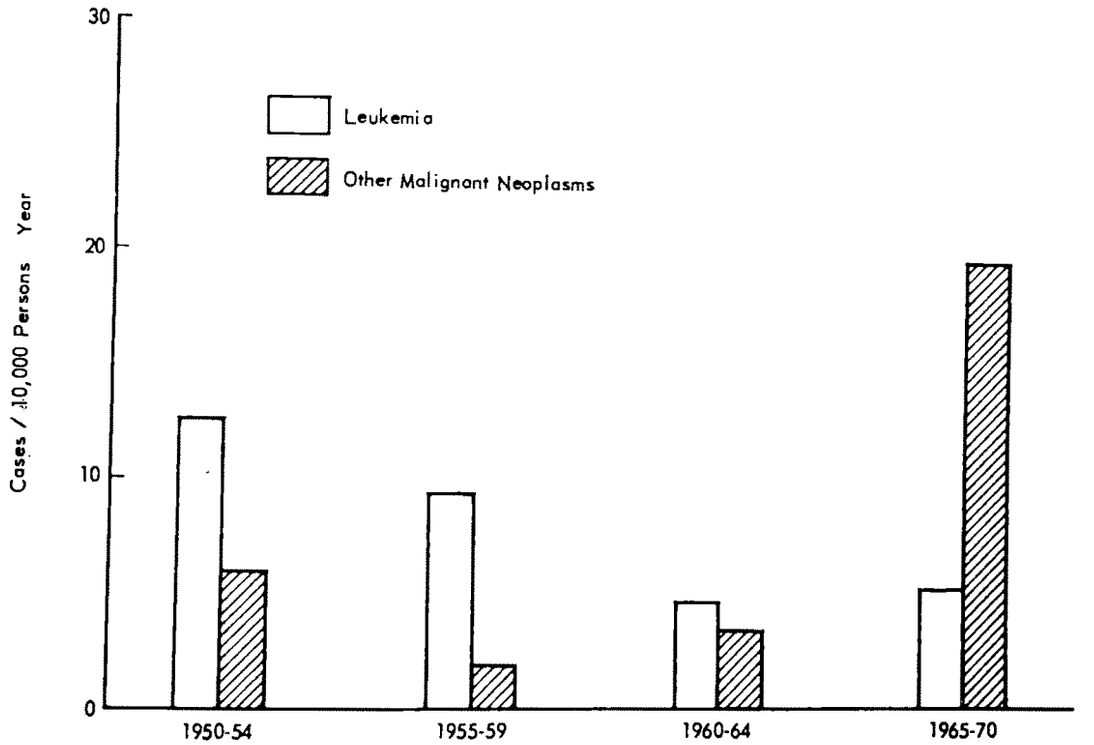


FIG. 3. Excess mortality per 10,000 persons per year in 200+ rad dose group by time period. Deaths from leukemia and other malignant neoplasms, 1950–1970. (Courtesy of S. Jablon and H. Kato,[21] and *Radiation Research.*)

were equally induced by intrauterine diagnostic radiation, the likelihood of an increase in frequency of all cancers by approximately 50 per cent has been challenged by other investigators.[31]

The difficulty with all of these epidemiologic studies is that a large number of factors can complicate the indications for obtaining the radiologic study in the first place and it is almost impossible to select controls in such a way that they will be beyond criticism. Despite these difficulties, however, the evidence emerging is that total body irradiation, even in very low doses, may be carcinogenic.

DATA ON RADIOLOGISTS

Data on effects of total body irradiation of radiologists should be carefully evaluated with reference to when the study was published. One such study published in 1948 shows a higher incidence of leukemia among American radiologists than among any other specialists between 1938 and 1942. In cancer incidence during this period, however, radiologists trailed dermatologists, neurologists, and psychiatrists.[12] A study by Shields Warren published in 1945[57] showed that American radiologists have a shorter life span than other American physicians by about 5 years. Brown and Doll,[8] however, showed that there was no difference in life span between radiologists and non-radiologists in Great Britain.

A significant excess of deaths from cancer did occur among those practicing radiology in Britain before 1921, when radiation protection standards were first established. These excess deaths were due mainly to tumors of the skin and pancreas and to leukemia. But no excess mortality from cancer was found in British radiologists who entered their specialties after 1920.

Comparing members of the Radiological

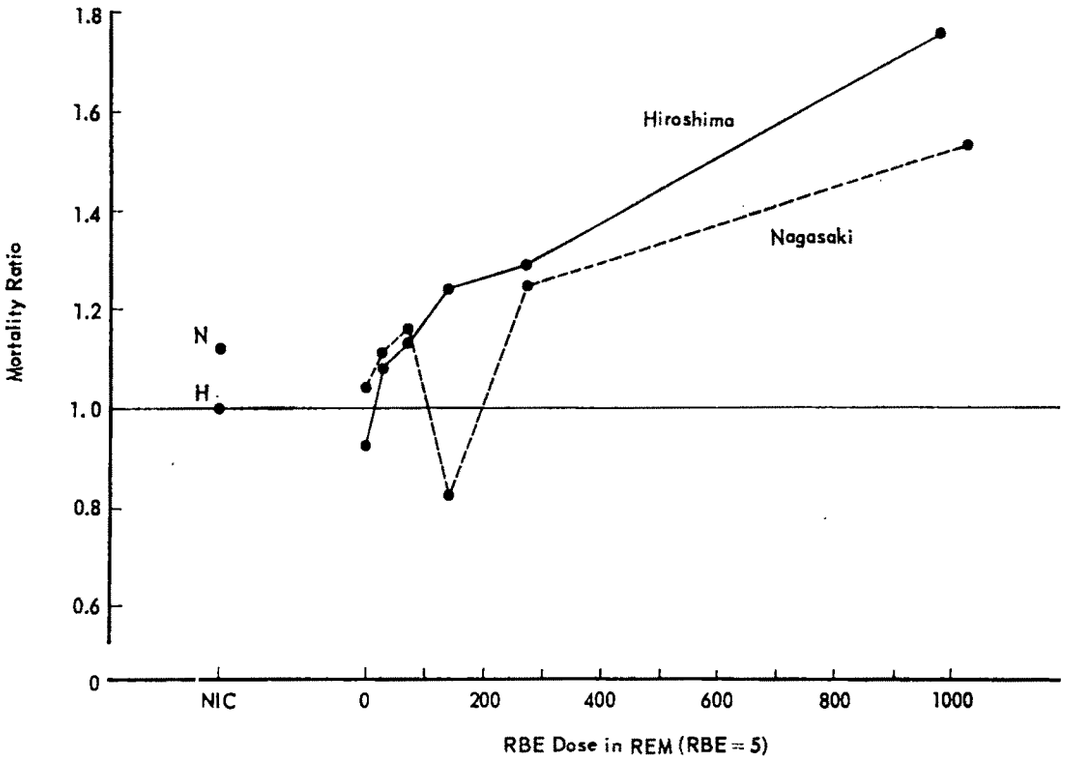


FIG. 4. Mortality ratios for all malignant neoplasms except leukemia. (Courtesy of S. Jablon and H. Kato,[21] and *Radiation Research.*)

Society of North America with members of the American Academy of Ophthalmology and Otolaryngology, Seltser and Sartwell[46] showed an increased incidence of death from leukemia among American radiologists from 1935 to 1954, but no excess occurred in the period between 1954 and 1958. No excess mortality among radiologists in the age class 35 to 49 years occurred in the period 1945 to 1958, although older radiologists practicing in the period 1935 to 1945 showed a decreased life span of close to 5 years compared with ophthalmologists.

On the basis of evidence available thus far, there appears to be no excess danger to radiologists and technicians from radiation today, provided that they follow the recommendations of the ICRP in their work, keeping the total body exposure to less than 5 rem per year.

LATE SOMATIC EFFECTS OF PARTIAL BODY IRRADIATION

Effects of partial body irradiation are of particular interest to diagnostic radiologists, since with proper techniques only parts of the patient's body are exposed. But most data in this field too are based on doses considerably larger than those used in diagnostic radiology. Even so, it appears that when part of the skeletal bone marrow in RF mice is shielded from radiation, the production of both myeloid and lymphatic leukemia can be inhibited.[54]

In a study of children with tinea capitis infections treated for epilation with large doses of x radiation, 4 cases of leukemia occurred among 2,404 treated patients compared with none among 1,540 controls.[1] Doll and Smith also report increased mortality from leukemia after radiotherapy for ankylosing spondylitis.[11] The doses admin-

istered were considerably higher and the fields much larger than the ranges used in diagnostic radiology, even with repeated examinations.

Other cancers have also been produced experimentally by partial body irradiation. It appears, however, that radiation is usually carcinogenic only if the organ, such as the mammary gland, is in the direct field of radiation.[6]

In a study of women with tuberculosis treated with artificial pneumothorax and frequently checked by fluoroscopy between 1940 and 1949, 13 out of 271 patients developed carcinoma of the breast in comparison with only 1 out of 570 patients in the non-fluoroscoped group. The doses were considerably in excess of those in conventional diagnostic radiology.[28]

A similar increase in cancer of the breast was found in the women victims of the atomic bomb explosions exposed to doses of over 90 rem.[56] It is interesting that extreme fractionation of the large dose administered to the breasts of fluoroscoped women had carcinogenic effects as great as the almost instantaneous delivery of radiation from the atomic bomb explosion. This indicates that at least for carcinoma of the breast there is no indication of a profound reduction in risk with decreased dose rate.

Increased mortality from carcinoma of the lung, as well as from other cancers, was reported after radiotherapy for ankylosing spondylitis.[11] Another study showed a linearity of response for benign thyroid neoplasms down to relatively low doses, above 20 rad.[20] Carcinomas of the thyroid, however, have been found only with radiation doses exceeding 100 rad.

GENETIC EFFECTS OF RADIATION

Genetic effects of radiation have raised even more of a public outcry in this country than somatic effects. This is understandable, particularly in view of the fact that the United States leads the rest of the civilized world in the level of the genetically significant dose (GSD) to its population. In 1964, the population GSD in the United States was 55 mrem/year, although the figure was seemingly reduced to a more acceptable 36 in 1970.

In 1956 the National Academy of Sciences-National Research Council's Committee on Biological Effects of Atomic Radiation introduced the concept of regulation of the over-all average dose to the population. Its recommendation was that the average individual should be exposed to less than 10 rad during his reproductive span (an average of 30 years).[4] The committee included medical radiation in its recommendations and estimated it to be approximately half of this 10 rad limit. The limit was extrapolated predominantly from work on *Drosophila* and laboratory mice and the recommendations were based on the following concepts: (1) any dose of radiation involving reproductive cells can produce mutation; (2) mutations are usually harmful; (3) the number of mutations occurring is proportional to the dose; (4) linear extrapolation from a high dose provides a valid estimate of effects of low doses; and (5) the effect is independent of the rate of irradiation and of spacing between exposures.

It is valid to assume that mutations are generally undesirable, although undoubtedly a certain number that have occurred over millions of years have been responsible for evolution and survival, as well as the demise of many species.

The assumption of complete linear extrapolation from high dose rate data appears to be wrong. From Russell's data on mouse spermatogonia and oocytes, it seems that radiation doses delivered at 0.009 rad per minute produced only from one-third to one-fourth as many mutations as did the same doses delivered at 90 rad per minute.[44] The dose rate effect was even more significant in oocytes.

Mechanisms have been worked out by which some radiation damage can be repaired in the cell after irradiation.[14,41] One important mechanism of x-ray damage in-

volves breaks in the DNA strands that can be repaired enzymatically. During repair of damage produced by x rays and by many other kinds of damage, incorporation of tritiated thymidine can be demonstrated in cells that are not in S phase of the cell cycle. This unscheduled DNA synthesis, easily demonstrable by autoradiography, is presumed to reflect a form of DNA repair. It has been demonstrated in spermatogonia in mice and humans as well as in many other cell types.[9,24]

Premutational repair after irradiation is believed by some[44] to be responsible for the production of fewer mutations when radiation is given at a lower dose rate or at more widely spaced intervals than when the same dose is given more rapidly. But there is some controversy as to whether or not the mutations studied are changes in base sequence of DNA or are merely chromosomal rearrangements.[59]

Ionizing radiation is capable of breaking chromosomes, although some of them may rejoin, leaving no effect. Others may reattach themselves in various ways, leading to abnormalities such as translocation, deletion, etc. Dicentric chromosomes are an example of this type of disturbance.

These changes are 2-hit aberrations that are subject to intensity or fractionation effects because of possible intercurrent repair between hits, which therefore decreases the chances for interaction. It must be emphasized, however, that most of the understanding of the effects of radiation on inducing mutations comes from relatively high doses in fruit flies and in mice, which have been shown to be considerably more sensitive than fruit flies.[26,44,59]

There are no definitive, precise genetic data for humans, even at high doses. The precautions recommended by committees are based on extrapolation from experimental data. On the basis of the data from Hiroshima and Nagasaki, it was suggested that at 50 rem a mutation rate effect equal to twice the spontaneous rate occurred.[13] With chronic exposure this doubling dose could be greater.

In summary, it appears that one cannot deny that there is a definite risk of radiation-induced mutations even in the diagnostic range. The exact incidence is extremely difficult to calculate for humans. The dose of radiation to patients in the reproductive age should therefore be kept as low as possible. It is an interesting thought that even though the risk may be acceptable for a particular individual because valuable diagnostic information may be forthcoming, the price of this risk will be paid by the progeny and not by the individual who is obtaining the benefit. Since most mutations are recessive and not manifested in the first generations, this price may not be paid for some time.

RADIATION DOSE AND BENEFITS OF DIAGNOSTIC EXAMINATIONS

Thus far in the discussion it has repeatedly been emphasized that most data on radiation carcinogenesis referred to doses above the diagnostic range. What is the diagnostic range? It must first be pointed out that it varies a great deal and depends on the skill of the operator, the technique used, and particularly whether collimation restricting the radiation to the patient is employed.

The order of magnitude of the average doses can be understood from tables published by the Atomic Bomb Casualty Commission. It is important to define the dose according to the anatomic area: surface dose, gonadal dose, or bone marrow integral dose. Table II shows some data obtained from this report. Data from our department[45] show that the doses to the bone marrow, while not large, are appreciable (Tables III and IV).

Diagnostic radiation procedures continue to increase, both in frequency and complexity[38] (Fig. 5). Widespread use of such procedures by the medical community despite the knowledge of radiation risks attests to the benefits derived from them. No precise data as to the amount of benefit derived, however, are available.

A study by Langston and Janower[25]

TABLE II

DOSE FROM ROENTGENOGRAPHY AND FLUOROSCOPY, DEPARTMENT OF RADIOLOGY, ATOMIC BOMB CASUALTY COMMISSION

Site of Examination	Projection	Average Thickness (cm.)	Film Size (inch)	kvp.	mas.	Added Filtration (mm. Al)	FFD (inch)	Bone Marrow Integral Dose (gm.-rad)	Gonadal Dose (mrad)		Surface Dose (mrad)
									Male	Female	
Chest	PA	21	14×17	100	5	2.5	72	1.73	0.02	0.04	9.21
	Lateral	32	14×17	110	15	2.5	72	3.29	0.03	0.08	37
	Lordotic	23	11×14	100	10	2.5	72	1.6	0.02	0.02	18
	Bucky PA	20	14×17	100	40	2.5	72	14	0.16	0.32	74
	Bucky Lateral	30	14×17	110	80	2.5	72	18	0.16	0.43	200
Abdomen	AP	17	14×17	100	20	2.5	40	17.7	11.6 (6.59)	51.1	159
	Lateral	27	14×17	120	60	2.5	40	57.2	9.77	61.5	820
Upper gastrointestinal series	Fluoroscopy (image)	17		90+	PHT	3.0		7.21/min.	0.348/min.	12.8/min.	328/min.
	Spot	17	8×10	90		3.0		1.35	0.07	2.68	101
	AP (survey film)	17	14×17	100	20	2.5	40	17.7	11.6 (6.59)	31.1	159
	PA	17	14×17	120	20	2.5	40	39.0	7.54	33.1	265
	RAO 45°	22	11×14	120	30	2.5	40	46.5	3.20	29.6	400
	RAO 60°	26	11×14	120	40	2.5	40	34.7	3.65	24.7	413
Barium enema examination	AP (survey film)	17	14×17	120	20	2.5	40	75.5	60.2	132	675
	Fluoroscopy (image)	17		90+	PHT	3.0		30/min.	11/min.	140/min.	480/min.
	Spot	17	8×10	90		3.0		5.90			110
Intravenous pyelogram	AP (abdomen, KUB)	17	14×17	120	30	2.5	40	75.5	60.2 (17.9)	132	675
	AP (bladder)	20	14×17	120	30	2.5	40	102	181	105	659
	Tomogram	17	11×14	120	20	2.5	40	33	12	80	450

FFD = focus film distance; PA = posteroanterior; AP = anteroposterior;
RAO = right anterior oblique; KUB = kidney, ureter, bladder;
PHT = photo-timed exposure.

surveying 762 consecutive radiologic examinations performed in the emergency ward of Massachusetts General Hospital showed that 26 per cent of the examinations confirmed the presence of significant pathology. Roentgen examinations requested for medicolegal purposes, such as skull examinations, had a very low incidence of positives. Of 55 skull examinations in this study, only 1 was positive and the patient required no treatment other than observation. The authors came to the conclusion that the figure of 26 per cent incidence of over-all radiologic abnormality could be

TABLE III

VERTEBRAL MARROW DOSE
(rad at mid-field)

Examination	High	Average	Low
Upper gastrointestinal	3.4	1.6	0.61
Barium enema	2.3	1.3	0.47
Intravenous pyelogram	0.74	0.31	0.11
Aortogram (arch)*	3.0	2.2	0.89
Aortogram (abdominal)†	41.	11.	1.0

* With selective carotids.
† Some with selective renal and hepatic arteriograms and superselective pancreatic studies.

TABLE IV

INTEGRATED VERTEBRAL MARROW DOSE
(gm.-rad)

Examination	Low	Average	High
Upper gastrointestinal	99	268	537
Barium enema	130	284	422
Aortogram (abdominal)*	176	1,144	3,680

* Some with selective renal and hepatic arteriograms and superselective pancreatic studies.

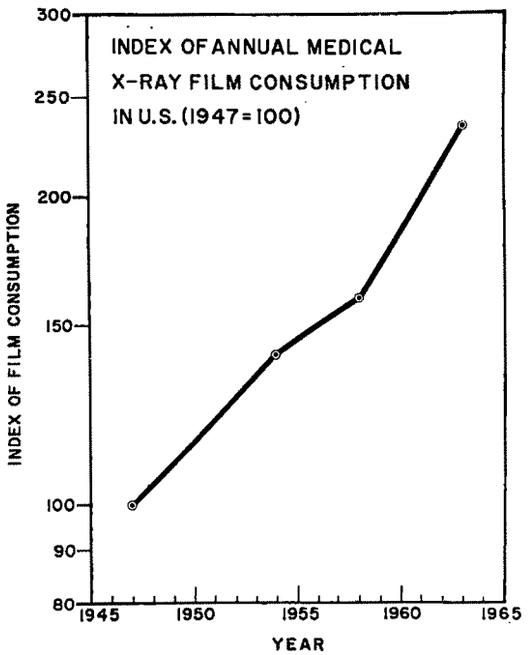


Fig. 5. Index of medical x-ray film consumption, calculated from data on the gross square footage of x-ray film produced annually in the United States minus film diverted for industrial and dental uses and adjusted for film exported and imported (from "Protecting and Improving Health through the Radiological Sciences"[39]).

increased to 33 per cent if the patients had had a careful physical examination by a physician and if skull and spine roentgenograms obtained only for legal protection and without clinical indications were excluded.

In an excellent editorial, McClenahan[27] questions whether the 44 per cent increase of x-ray film shipped in the United States between 1958 and 1963, as compared with the population increase of only 14.3 per cent during the same period, results from really necessary examinations or from a large number of routine examinations and examinations to satisfy lawyers. It will be necessary to educate lawyers as well as our colleagues who order unnecessary examinations about the dangers of radiation. This shotgun approach of ordering x rays to satisfy lawyers can be likened to endangering many innocents to apprehend an occasional culprit.

The same conclusion is reached by Bell and Loop,[3] who developed a prospective questionnaire for house officers in emergency rooms in 2 hospitals in Seattle. An analysis of 1,500 skull x-ray examinations for appearance of fractures demonstrated that if patients were divided into high-yield and low-yield groups on the basis of 21 high-yield clinical findings, only 1 of the 93 patients with fracture would not have had his roentgenograms taken. This patient with a skull fracture would not have had his therapy significantly altered because the fracture was demonstrated on x-ray study. Four hundred and thirty-four patients without fracture would not have had their skull roentgenograms taken, representing 29 per cent of all skull examinations.

Similarly, a 5 year follow-up of routine survey roentgenograms of the abdomen on 500 consecutive patients over 40 years of age showed that only 4 per cent developed symptoms relevant to the reported abnormal roentgen findings. The authors conclude that routine survey roentgenograms of the abdomen are not indicated even in patients being admitted to a hospital.[17]

Survey roentgenograms of the chest are probably also not indicated, as the low yield of positive diagnosis in unselected populations is not worth the risk of exposure. On the other hand, in populations where there is a high incidence of disease, x-ray surveys are probably still useful. For example, in a review of control of tuberculosis in 1967, Mitchell states that x-ray surveys still have a place in populations of high incidence.[32] Family contacts of newly discovered open cases of tuberculosis are the most productive source for detection (15–20 cases per 1,000 x-ray examinations). In the same year, Kent reported outbreaks of active tuberculosis in the United States Navy. The tuberculosis rate on ships and shore had increased from a rate of 16.3 per 100,000 in 1963 to 26.5 per 100,000 in 1965.[23] Other fruitful areas for such surveys are urban slums, jails, mental institutions, and nursing homes.[32]

Similarly, if groups are carefully selected among men over the age of 45, particularly smokers, periodic chest roentgenograms on asymptomatic individuals are currently the most promising way of diagnosing lung cancer early enough to effect a cure.[19]

Survey examinations of the stomach are of value in populations with a high incidence of gastric cancer, such as the Japanese. In the United States this type of survey examination is not indicated.[2]

The true effectiveness of diagnostic radiology is difficult to evaluate, although radiologic examinations certainly are central in the diagnostic work-up of patients. Currently, a Committee of the American College of Radiology is evaluating the effectiveness of x-ray examinations. This work probably will take some time and its results should be important. At the University of California, San Francisco, a small pilot study was undertaken to determine the influence of x-ray examinations during 2 randomly selected 24 hour periods on the subsequent treatment and handling of 600 patients. The greatest difficulty in evaluating such a study is that clinical decisions are often highly subjective and no 2 physicians follow the same indications.

CONCLUSIONS AND RECOMMENDATIONS

The conclusions of this long discussion are remarkably simple. There is a risk from diagnostic radiation to the patient, to the operator, and to the progeny of patients. Despite extensive studies, experimental and epidemiologic, including the large and coordinated studies on the victims of atomic bomb explosions, no precise relationship has been established between doses of radiation below 20 rad and somatic or genetic effects in humans (the 20-rad figure is conservative). The dose effect curves may be curvilinear, there may be a threshold, but at present the evidence is inadequate for adoption of firm conclusions. To safeguard populations and to protect them from our ignorance, a conservative approach of assuming linearity to the lowest dose is the only logical and responsible policy. It is important, therefore, to keep radiation from all sources to the lowest possible level.

It is at this point that you may expect some numbers and precise limits. There are none to be given. If the examination is not indicated, the number is zero. If it is indicated, the dose should be the lowest needed for a diagnosis. The recently enacted federal regulations about x-ray equipment standards, the state laws for periodic inspection of equipment and examinations of operators are steps in the right direction. Strict adherence to ICRP and NCRP standards is needed.[30,38,40]

Radiologists and physicians should dispense with routine roentgen examinations and only perform or order those that are medically indicated in the particular patient. Routine views for every examination should be reduced to a minimum; additional views should be obtained as indicated on the basis of the few views obtained and only under control of a knowledgeable physician. A great deal of care should be given to perfecting technique; as my colleague, Dr. Earl Miller, suggests, "Every radiologist should throw out the bright light used to scan overexposed films." Overexposed films mean an unnecessary excess in patient dose. Further studies are needed to determine the detail necessary on the films to make them diagnostic, since the purpose of the examination is to make a diagnosis and not to obtain beautiful films. Faster screens and faster film will undoubtedly be developed and result in further savings in dose.

As many examinations are repeated because the previous films are not available for viewing, perhaps Dr. Richard Greenspan's suggestion that each patient be entrusted with his own films once he is discharged from the hospital or from the office has merit. Certainly the patient has more at stake to preserve and safeguard his own films than a filing room, which usually is in some type of trouble. Roentgenograms that have been interpreted but temporarily mislaid should not be repeated to satisfy the referring physician's curiosity. This should

be done only if immediate re-examination will affect the handling of the patient and the words of the report cannot substitute for the image.

Lastly, as radiologists we must assume the role of consultant and not just pay lip service to this concept. No examination in an X-ray Department should be performed unless first approved by a radiologist who has carefully screened the indications and recommended that study which will have the greatest effectiveness and give the least dose to the patient.

A procedure for handling of most diagnostic x-ray examinations should be as follows:

A. Decision on examination and type
   1. Look at the request, which should contain the reason for the examination and relevant information.
   2. Look at the chart.
   3. See the patient and obtain a short history; examine the patient if necessary.
   4. Decide whether an examination is needed.
   5. Select the best examination.

B. Examination conducted with the smallest number of views

C. Tailoring of examination
   1. Inspect the films.
   2. Order additional views if needed.
   3. Report as consultant.

Radiologists must have courage to protect the patient from unnecessary examinations and knowledge of clinical medicine and other diagnostic modalities. The persistence of unnecessary pelvimetries still being performed is pressing evidence that a change of attitudes is needed.

We will have to change some of our working habits and make efforts to re-educate our colleagues. It will often be less than peaceful, but in the words of one of our philosophers: *If you cannot stand the heat, get out of the kitchen.*

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DECISION PROCESSES AND OBSERVER ERROR IN THE DIAGNOSIS OF PNEUMOCONIOSIS BY CHEST ROENTGENOGRAPHY*

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I. INTRODUCTION

IN 1969, the Congress of the United States enacted the Federal Coal Miners Health and Safety Act (PL-91-173) providing certain benefits to coal miners with pneumoconiosis. The law specifies that underground miners presenting x-ray evidence of pneumoconiosis and who subsequently exhibit some degree of disability by pulmonary function tests are to be compensated at levels related to their disability. Moreover, x-ray changes characteristic of massive disease constitute irrefutable evidence of disability.

The administration of the law has been placed under the National Institute of Occupational Safety and Health, Public Health Service, for miners actively engaged in mining operations and under the Bureau of Disability Insurance, Social Security Administration, for retired or disabled miners and for widows of miners whose deaths were attributed to pneumoconiosis.

The operators of mining facilities were required to arrange for each active miner to have a chest roentgenogram by July 1, 1971 and to have additional roentgenograms at periodic intervals thereafter. In order to assure the availability of an adequate pool of professional manpower to carry out the interpretation of these roentgenograms, the National Institute of Occupational Safety and Health in cooperation with the American College of Radiology gave a series of short, intensive courses on the diagnosis of pneumoconiosis for radiologists and chest physicians who wished to participate in the program.

One of the provisions of the law permits a miner to appeal an adverse decision of his case. Hence, the National Institute of Occupational Safety and Health and the Bureau of Disability Insurance have established means whereby the findings in any case may be reviewed. Such a review is also sometimes undertaken when the agency has some reason to question the validity of the x-ray findings or the results of the pulmonary function tests. It has been in the review processes of the Social Security Administration that we have become involved in the application of the law.

In our consultation and review roles, it became evident to us very early that the interpretation of chest roentgenograms for pneumoconiosis presents many problems similar to those encountered by Yerushalmy,[8,9] and Garland[1] in the late 1940s and 1950s when they examined the decision processes and observational error involved in the diagnosis of minimal pulmonary tuberculosis by chest roentgenography. It will be recalled that these workers found considerable variation in the readings made by different physicians interpreting identical sets of films and by a given physician reinterpreting films he had examined at a prior time. So too, we noted substantial variation in the readings of miners' chest roentgenograms for pneumoconiosis made by radiologists and chest physicians in the field and those made by ourselves in review.

The existence of such interpretive differences is characteristic of all diagnostic modalities. Their causes have been exten-

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sively studied by Swets,[7] Lusted[4] and others and are related to the inability of available diagnostic criteria to completely separate roentgenographically those individuals with disease from those without. The patterns of normality and of the pathologic state overlap each other to such an extent as to cause some cases to be interpreted as having disease when no disease exists (false positive interpretations) and some cases to be interpreted as not having disease when it is actually present (false negative interpretations). As one might expect, the decision processes for separating normal and pathologic states are generally less certain among readers whose experience is limited. This is particularly so in situations where the diagnostic criteria are difficult to quantify, as is generally the case in radiologic situations.

Studies of the decision-making process have shown that in a given diagnostic problem, the percentages of false positives and false negatives interpreted by a group of equally qualified readers bear an inverse relationship to each other. Individuals who have low false negative scores tend to exhibit a relatively high false positive response, whereas those with high false negative scores exhibit a relatively low false positive response. As an individual acquires more and more experience, his false positive and false negative scores tend to diminish.

The tendency of diagnostic procedures such as chest radiography to yield not inconsiderable numbers of false positive and false negative readings has been of concern to many physicians, and several methods have been proposed to minimize this characteristic. One of these is the process of double reading by independent interpreters. The review mechanism of the Bureau of Disability Insurance is a variation of this technique.

II. CRITERIA OF DIAGNOSIS

The diagnostic criteria used by the National Institute of Occupational Safety and Health and the Bureau of Disability Insurance for the determination of pneumoconiosis from chest roentgenograms are those developed in 1958 by the International Labour Organization (ILO)[2] and revised jointly in 1967 at Cincinnati by the International Union Against Cancer (UICC), Committee on Asbestos and Cancer, and the Roentgenologic Panel of the National Center for Urban and Industrial Health, the United States Public Health Service.[3] These criteria are based upon the fact that pneumoconiosis is a disease characterized by the development of granulomatous nodules in the supporting reticulum of the lungs which manifest themselves roentgenographically as multiple rounded or irregular opacities diffusely distributed throughout the lung fields. When the opacities are small, 3 criteria of diagnosis are used: (a) opacity profusion, *i.e.*, the number of opacities observed per unit area of the chest film; (b) opacity shape; and (c) opacity size.

The UICC/Cincinnati classification divides the profusion criterion into 4 major categories, each of which is further divided into 3 minor subgroups. The 4 major categories include: (a) Category 0 in which the films are judged to be normal, *i.e.*, small rounded or irregular opacities are absent or less profuse than in the following category; (b) Category 1 in which small rounded or irregular opacities are definitely present but are relatively few in number; (c) Category 2 in which the opacities are more numerous but in which the pulmonary vascular patterns are still visible; and (d) Category 3 in which the opacities are present in sufficiently large numbers to obscure the pulmonary vascular markings either partially or totally. The 3 subgroupings of each major category have been introduced into the classification to provide a means for the reader to report findings that are slightly less than, equal to, or slightly greater than, those represented by the major category alone. In all, therefore, the profusion criterion is divided into a total of 12 categories ranging from complete normality to moderately severe disease. These 12 categories are designed for reporting purposes by the codes 0/ to 3/4 as shown in Table 1. In a

given case, profusion levels may vary widely from region to region of the roentgenogram. In such an instance, the profusion value assigned to the case is that obtained when the findings are averaged over the zones predominantly affected.

The UICC/Cincinnati classification divides opacity shape for small lesions into 2 categories: (A) small rounded opacities; and (B) small irregularly shaped opacities. For small rounded opacities, the criterion of opacity size is divided into 3 categories: (a) opacities up to 1.5 mm. in diameter; (b) opacities between 1.5 and 3 mm. in diameter; and (c) opacities between 3 and 10 mm. in diameter. For small irregular opacities, size is classified as: (a) fine irregular or linear opacities; (b) medium opacities; and (c) coarse (blotchy) opacities.

For large opacities greater than 10 mm. in maximum dimension, opacity size is divided into 3 categories: (A) opacities 1 to 5 cm. in diameter; (B) opacities larger than A but not greater than one-third of the area of the right lung field; and (C) opacities larger than B.

In the application of the foregoing diagnostic criteria, the Bureau of Disability Insurance depends entirely on the profusion criterion for the separation of cases positive for pneumoconiosis from those that are negative. Cases interpreted as falling into Category 0 (the so-called normal category) or into one of its subgroups (*i.e.*, 0/, 0/0 or 0/1) are regarded as being free of the disease. Cases which fall into Categories 1, 2 or 3 or their subgroups (opacities definitely present) are regarded as being positive for pneumoconiosis. Little or no use is made of opacity size and shape in separating positives and negatives. These criteria are used to evaluate severity of disease; for example, all cases with large opacities judged to be due to pneumoconiosis qualify for disability benefits regardless of other findings.

If pneumoconiosis were the only condition which produces small rounded or irregular opacities in chest roentgenograms, the diagnosis of the disease would be relatively simple. Unfortunately, other conditions, both normal and abnormal, may produce such patterns and frequently are difficult to differentiate from pneumoconiosis. For example, the images of blood vessels projected on end present rounded opacities in the chest roentgenogram. Their profusion, however, is generally much less than that observed in pneumoconiosis. Moreover, blood vessels seen on end are likely to be much less uniform in size than the opacities produced by pneumoconiosis and branching patterns are frequently visible radiating from them.

Table I

CODES USED IN REPORTING THE PROFUSION STATUS OF PNEUMOCONIOSIS OPACITIES IN CHEST ROENTGENOGRAMS ACCORDING TO THE UICC/CINCINNATI CLASSIFICATION

Major Category	Minor Categories		
	<	=	>
0	0/	0/0	0/1
1	1/0	1/1	1/2
2	2/1	2/2	2/3
3	3/2	3/3	3/4

Histoplasmosis and miliary tuberculosis also produce multiple small opacities in the chest roentgenogram which may be confused with those of pneumoconiosis. However, these opacities are frequently more dense than those produced by pneumoconiosis due to calcification of the underlying lesions.

As individuals grow older, the vascular patterns recorded on chest roentgenograms become thicker and may exhibit irregular, somewhat nodular configurations that either may be confused with the opacities of pneumoconiosis or may obscure them. This is particularly so if the individual has been a heavy smoker, has had numerous pulmonary infections or is in congestive heart failure and some edematous infiltration of pulmonary tissues is present during the roentgenographic process.

A number of other instances may be cited where the presenting roentgenographic patterns may interfere with the evaluation of

pneumoconiosis. Together they constitute so-called "ordered noise" which interferes with the decision processes involved in the detection of the disease. Consequently, when the extent of the pneumoconiosis is minimal, there are few situations in diagnostic roentgenology where the differentiation of the normal from the abnormal is more difficult.

III. THE DECISION PROCESS IN PNEUMOCONIOSIS

The manner in which interfering patterns affect the decision processes and observer error in the interpretation of chest roentgenograms for pneumoconiosis may be illustrated by the following. Let us first consider the profusion of small, rounded or irregular opacities (*i.e.*, the number of opacities per cm.^{2}) in a representative sample of roentgenograms of individuals who are free of the disease. Curve A (Fig. 1), plotting the probability of one's observing a given profusion level, might characterize the data resulting from such a study. Let us now consider the profusion of similar opacities in the roentgenograms of individuals who have pneumoconiosis. Because profusion levels are higher in such cases, the corresponding probability distribution generated by these cases might be characterized by Curve B. It will be observed that the 2 curves overlap and, quite clearly, uncertainty of diagnosis will prevail for those cases included in the region of overlapping. For example, consider an interpreter who selects his operating point for the separation of cases he will call positive for pneumoconiosis from those he will call negative at a profusion level of x_c. The cases to the right of x_c in region 1 will be called positive for the disease. Of these, the cases under the unshaded portion of Curve B will be correctly diagnosed; that is, they will be true positives. However, those cases included under the shaded portion of Curve A (a) will also be called positive in spite of the fact that they actually are free of the disease; such cases will therefore be false positives.

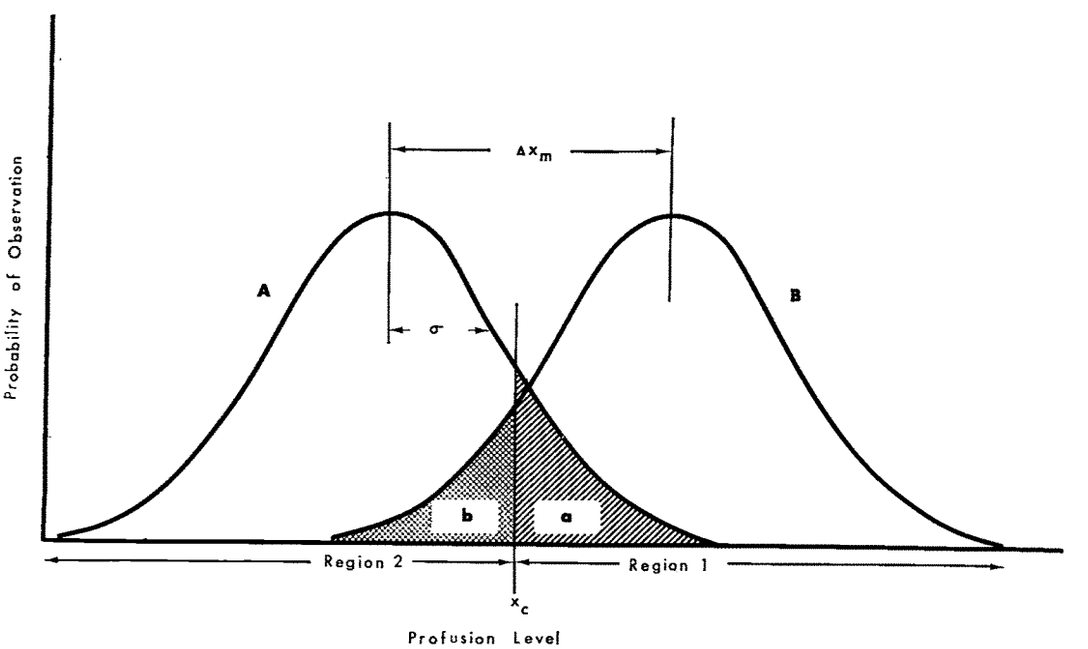


FIG. 1. Representation of the decision problem in pneumoconiosis. Hypothetical population distributions in which the ordinate depicts the probability of one's observing a given profusion level in a population free of pneumoconiosis (curve A) and in a population with pneumoconiosis (curve B).

The cases to the left of x_c in region 2 will be interpreted as normal. Of these, the cases under the unshaded portion of Curve A will be correctly diagnosed and hence will be true negatives, whereas those under the shaded portion of Curve B (b) must represent false negative interpretations, since the disease is actually present in these cases.

It will be evident from an examination of Figure 1 that the percentages of false positive and false negative interpretations will depend upon where the operating point, x_c is placed. If it is placed to the left of the position shown, the number of false negatives will diminish but at the expense of an increasing number of false positives. On the other hand, if the operating point is moved to the right, the number of false positives will diminish but at the expense of an increasing number of false negatives.

The percentages of false positive and false negative interpretations will be greatly influenced by the amount of overlapping of the 2 probability distributions shown in Figure 1. Overlapping will increase as the difference in the means of the 2 distributions, Δx_m, becomes smaller and diminish as Δx_m becomes greater. Furthermore, overlapping will increase as the standard deviation, σ, of each distribution becomes larger and decrease as σ becomes smaller. The ratio of $\Delta x_m/\sigma$ is called the index of detectability, d'.

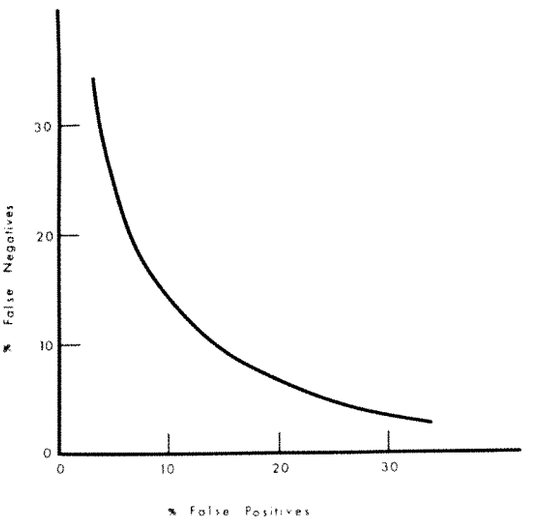


Fig. 2. Hypothetical curve illustrating reciprocal relationship between percentage false negative and false positive interpretations of chest roentgenograms for pneumoconiosis.

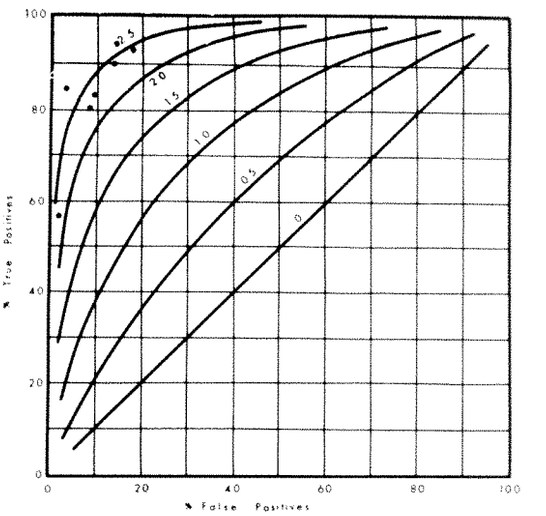


Fig. 3. Receiver operator characteristic (ROC) curves illustrating manner in which values of the index of detectability, d', affect percentage true positive and false positive relationships.

The reciprocal relationship prevailing between the percentage false positive and false negative interpretations as one moves the operating point, x_c, along the decision axis is illustrated graphically in Figure 2, where the percentage of false positives is plotted as a function of the percentage of false negatives for a number of different values of x_c. The characteristics of this curve are markedly influenced by the value of the index of detectability, d'. Figure 3 illustrates a series of curves (called receiver operator characteristic or ROC curves) in which expected true positive and false positive percentages are plotted for different values of d' when the diagnostic probability distributions are normally distributed and the values of σ are equal. It will be noted that when the value of d' is large, corresponding to conditions of minimal overlapping of the two distributions in Figure 1, false positive and false negative percentages are relatively small. When the value of d'

is small, corresponding to conditions when overlapping is substantial, false positive and false negative percentages are large.

It will also be observed that the loci of the several ROC curves plotted in Figure 3 are symmetric about a diagonal drawn from the upper left to lower right corners of the chart. This is characteristic of curves derived from diagnostic probability distributions that are normally distributed and in which the values of σ are equal. When these conditions do not prevail, the curves become asymmetric about the diagonal. Examples of ROC curves of both symmetric and asymmetric type have been illustrated by Lusted.[4]

IV. EXPERIMENTALLY DERIVED VALUES OF OBSERVER PERFORMANCE

In the preceding section, we have seen how the overlapping of the probability distributions of small rounded and irregular opacities in the chest roentgenograms of normal individuals and of individuals with pneumoconiosis causes an interpreter of such roentgenograms to make a number of false positive and false negative errors. If these probability distributions were known, one could predict the performance of a group of interpreters confronted with the problem of separating individuals with disease from those who are normal. Unfortunately, these distributions are not known. Even though profusion levels in films of normal individuals and of individuals with pneumoconiosis are amenable to measurement, the decision processes used in separating the normal from the abnormal are more complicated than the simple estimation of profusion level. For example, x-ray scatter, quantum mottle and random eye movements tend to make decision processes more difficult. Also, observers, as experience is gained, learn to recognize differences in opacity characteristics other than their profusion to increase their ability to distinguish between the opacities produced by pneumoconiosis and those produced by such other normal and abnormal situations as blood vessels seen on end, the interstitial fibrosis of smokers, etc. Hence, the true probability distributions on which decision processes actually rest are different from those illustrated in Figure 1, exhibiting perhaps more overlapping for the inexperienced reader and less overlapping for the experienced interpreter.

Even though the appropriate probability distributions are not known, it is often possible, as Lusted[4–6] has pointed out, to obtain an estimate of d' and thereby a measure of an observer's sensory capabilities to separate normal cases from those with pneumoconiosis by preparing a set of roentgenograms containing examples which are positive and negative for the disease in proportion to their numbers in the population and submitting them to the observer for interpretation. The roentgenograms must, of course, be of individuals whose disease, age and personal characteristics are similar to those in the population of interest, since these attributes may have a bearing on decision processes.

When the series of test roentgenograms has been interpreted and the observer's percentage true positive and percentage false positive scores calculated, his index of detectability may be estimated from Figure 3 or from tables published by Swets,[7] if the diagnostic probability functions are normally distributed. Moreover, depending upon where his data fall upon the receiver operator characteristic curve, a measure of his attitude at the time of reading may also be obtained. For example, if his percentage false positive score is high, he has been motivated by a desire to detect as many true positive cases as possible. On the other hand, if his percentage false positive score is low, he has been more concerned with the cost of his calling individuals who are free of the disease positive than of calling individuals who have pneumoconiosis negative.

To examine observer characteristics in the interpretation of chest roentgenograms for pneumoconiosis, we have prepared a set of 200 roentgenograms derived at random from those submitted to the Social Security Administration as a part of their responsi-

bility under the Federal Coal Miners Health and Safety Act. The age and geographic distributions of the individuals included in the study are shown in Tables II and III.

The profusion category of each case was determined by a process of independent readings by 5 radiologists experienced in the interpretation of chest roentgenograms for pneumoconiosis. Together they had a combined experience of 50 years following certification by the American Board of Radiology. Readings were made in accordance with the UICC/Cincinnati classification. After the readings were completed in each case, profusion values were averaged and where the reading of any radiologist of the group differed by no more than 2 minor profusion categories from the average, the case was classified as having this average profusion level. When a reading of any of the 5 radiologists differed from the average by more than 2 minor profusion categories, the case was reviewed jointly by the group and a consensus decision reached. In both instances, copies of roentgenograms prepared by the ILO to illustrate various profusion levels were available to assist in the categorization process. Table IV illustrates the distribution of profusion levels in the 200 cases selected.

The roentgenograms were then submitted to 7 radiologists for interpretation. For each observer, the interpretations were analyzed on the basis that any case given a profusion rating of 0/1 or below was regarded as negative by the observer and any case given a rating of 1/0 or greater was positive. True positive, false negative, true negative, and false positive percentages were then calculated.

The results of the study are shown in Table V, where it will be observed that the indices of detectability of the several readers ranged from 2.17 to 2.89. The points representing their true positive–false positive scores are shown in Figure 3. These points follow a generally symmetric ROC curve although their distribution is sufficiently dispersed to prevent one from being sure of this. Nevertheless, the data suggest that the readers' diagnostic probability functions are not far from being normally distributed.

The distribution of the points in Figure 3 also illustrates the variation in attitude exhibited by the several observers. It is of in-

TABLE II

AGE DISTRIBUTION OF INDIVIDUALS WHOSE CHEST ROENTGENOGRAMS ARE INCLUDED IN THE 200 TEST FILMS

Age	No. of Individuals
36–40	1
41–45	2
46–50	4
51–55	11
56–60	27
61–65	38
66–70	43
71–75	44
76–80	20
81–85	4
86–90	5
>90	1

TABLE III

GEOGRAPHIC DISTRIBUTION OF INDIVIDUALS WHOSE CHEST ROENTGENOGRAMS ARE INCLUDED IN THE 200 TEST FILMS

Geographic Location	No. of Individuals
Eastern Pennsylvania	47
Western Pennsylvania	109
West Virginia	11
Kentucky	26
Other	7

TABLE IV

DISTRIBUTION OF PROFUSION LEVELS IN THE 200 TEST FILMS

Profusion Category	No. of Cases
0/0	50
0/1	77
1/0	25
1/1	14
1/2	9
2/1	13
2/2	7
2/3	5

TABLE V

PERFORMANCE OF 7 READERS INTERPRETING SERIES OF 200 TEST FILMS FOR PNEUMOCONIOSIS

Reader	Per Cent True Positives	Per Cent False Positives	Index of of Detectability
A	83.3	9.4	2.25
B	94.4	14.1	2.66
C	80.6	8.6	2.24
D	93.1	18.0	2.38
E	57.0	2.3	2.17
F	84.7	3.1	2.89
G	90.2	13.3	2.41

terest to note that even though these attitudes varied widely, the fact that all of the points fall along a common locus (*i.e.*, a single ROC curve) indicates that the several observers used approximately similar diagnostic criteria in making their interpretations.

In practice not all observers will demonstrate d' values as high as those of the 7 readers whose data are shown in Figure 3. For example, one individual with long experience in radiology, but who has worked for several years in a government agency removed from radiological practice, demonstrated a d' value of 1.84 when he reviewed the test roentgenograms. Moreover, a group of several physicians each of whom read a section of the test series of roentgenograms and who collectively read the entire series, exhibited a composite d' value of 1.33. Such a performance indicates that the diagnostic criteria used by these readers were different and less sharply defined than those of the readers with higher d' values. Their relatively low score raises a question concerning their suitability for inclusion in a pneumoconiosis x-ray interpretation program without further training.

CONCLUSION

The foregoing results indicate a need for an examination which may be administered to physicians who wish to be included as interpreters of chest roentgenograms in the pneumoconiosis program. The set of test roentgenograms prepared for this study might be effectively employed for this purpose. Such an examination would assure only the inclusion in the program of physicians whose indices of detectability are relatively high. With such physicians, the mining community and the public could be assured that a maximum number of miners with pneumoconiosis will be detected at a minimum cost to the taxpayers who must support the program.

Currently, we are in the process of giving the test to more than 25 radiologists experienced in the interpretation of chest roentgenograms for pneumoconiosis. From these studies it is hoped that quantitative criteria may be developed, whereby the acceptability of a prospective candidate wishing to engage in the pneumoconiosis program may be determined.

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SOLITARY MASS IN THE LUNGS OF COAL MINERS*

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ROENTGENOGRAMS of 1,500 Pennsylvania coal miners who had worked underground more than 15 years showed one or more lung masses in 9.6 per cent of the anthracite miners and 3.8 per cent of the bituminous miners. Similar masses also occur in coal handlers who have never worked underground, especially in those employed in anthracite breakers. Most of the lesions are caused by progressive massive fibrosis (conglomerate pneumoconiosis, complicated pneumoconiosis, conglomerate anthrasilicosis). The masses may closely simulate a carcinoma, especially when solitary. The presence or absence of small nodules of simple pneumoconiosis is not especially helpful in the differential diagnosis because half the miners of both anthracite coal and higher rank bituminous coal have some roentgenographic evidence of simple pneumoconiosis after 15 or more years of dust exposure, and there is only fair correlation between the degree of nodularity in the lungs and the presence or absence of progressive massive fibrosis (PMF). In fact, in occasional cases of PMF, there is no nodularity on the roentgenograms, and the correct diagnosis would not be suspected in the absence of a work history.

Coal miners with a long occupational exposure often have some degree of pulmonary disability, regardless of the roentgenographic findings, but there is great individual variation.[4] As a group, however, they are not good operative risks and can ill afford unnecessary chest surgery or lung resection. At surgery, it may be difficult to differentiate between PMF and neoplasm, short of resecting the lung, and there may be such extensive fibrosis that evaluation of the entire lesion is technically difficult, particularly when the mass is in the hilar region or near the mediastinum.[6] For these reasons, any criteria which will help differentiate between PMF and tumor in this poor risk group would be of value. Fortunately, the incidence of lung cancer is no greater, and may even be less, in coal miners than in non-miners.[3]

OCCUPATIONAL HISTORY

It is uncommon to see PMF in a coal worker who has had less than 20 years of employment in or around mines, and among current miners we have seen only 1 case of PMF with less than 15 years of dust exposure.

Both the roentgen manifestations and the degree of pulmonary disability in Pennsylvania miners vary markedly with the geographic area. The differences appear to be best related to the amount of silica associated with the mining and handling of the various ranks of coal, rather than to any particular properties of the coal.[1,5] At autopsy, the hard coal (anthracite) miners of eastern Pennsylvania have 8 times as much silica in their lungs as the miners of low rank soft coal in southwestern Pennsylvania.[5] The hard coal (anthracite) miners have a greater tendency to develop nodular and conglomerate densities, often more marked in the upper lung fields, and the roentgenographic appearance is similar to that of pneumoconiosis caused by exposure to pure silica. In contrast, the miners of low rank bituminous coal in southwestern Pennsylvania have less tendency to develop nodules in the upper lung fields, but after long exposure may have irregular densities in the interstitial tissues, especially in the lower half of the lungs. They are much less likely to develop PMF than the anthracite miners. The miners of higher rank soft coal in central Pennsylvania are

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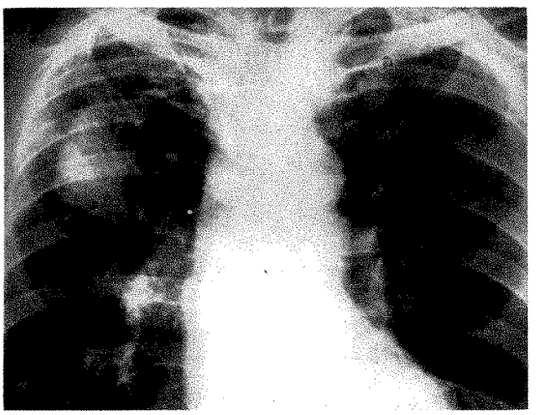


FIG. 1. Characteristic contour and density of progressive massive fibrosis (PMF).

intermediate between the above extremes. Thus, the geographic area, as well as the length of dust exposure, must be taken into consideration when there is a possibility that a lung mass might be caused by PMF.

DIAGNOSTIC ROENTGENOGRAPHIC FINDINGS

Shape of the Mass. PMF typically starts near the periphery of the lung where it often has a characteristic appearance. The most reliable finding on the frontal roentgenogram is a mass with a smooth, sharp, elongated lateral border paralleling the rib cage and often projected 1 to 3 cm. from the lateral costal margin. The medial margin of the mass is often ill-defined, in contrast to its sharp lateral border (Fig. 1). This typical lateral border was present in 22 of 50 cases of solitary lung masses in coal miners. No case with these characteristic features has proved to be malignant at surgery, at autopsy, or on follow-up, and we do not recommend surgery when this typical lateral border is present. Bateson[2] analyzed 80 cases of primary carcinoma of the lung. Only 22 of the cancers had a smooth well-defined border, and all of these showed at least slight lobulation. Contour drawings of 70 of his cases of carcinoma showed none with a border resembling the straight lateral margin of PMF.

In lateral or oblique projections of the chest, PMF tends to be thin, is often somewhat spindle-shaped, and frequently parallels the long fissure (Fig. 2).[6] This is the second helpful roentgenographic finding because carcinomas tend to be more spherical. If the lesion started in the lateral part of the lung, it will appear thin in the lateral projection, but if it started near the front or back of the lung, its thinnest dimension will be seen in one of the oblique projections.

Density. On the posteroanterior roentgenogram the density of an area of PMF is often not as great as one would expect if the lesion were spherical. This is to be anticipated since PMF tends to be flattened. This diagnostic sign is most helpful on survey studies when only a posteroanterior roentgenogram is available (Fig. 3).

Calcification. Four types of calcification occur in both coal workers' pneumoconiosis and silicosis. Eggshell calcifications are the best known but are uncommon, occurring in 1.3 per cent of 1,063 coal miners whose chest roentgenograms showed evidence of pneumoconiosis. All had worked 20 or more years in the mines. Eggshell calcifications usually indicate silica exposure, although they are occasionally seen in Boeck's sarcoid and following certain bacterial and

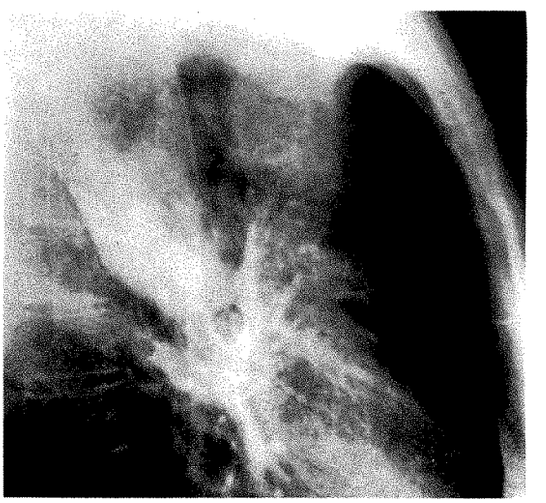


FIG. 2. On the lateral roentgenogram, PMF is typically thin. Carcinomas tend to be more spherical.

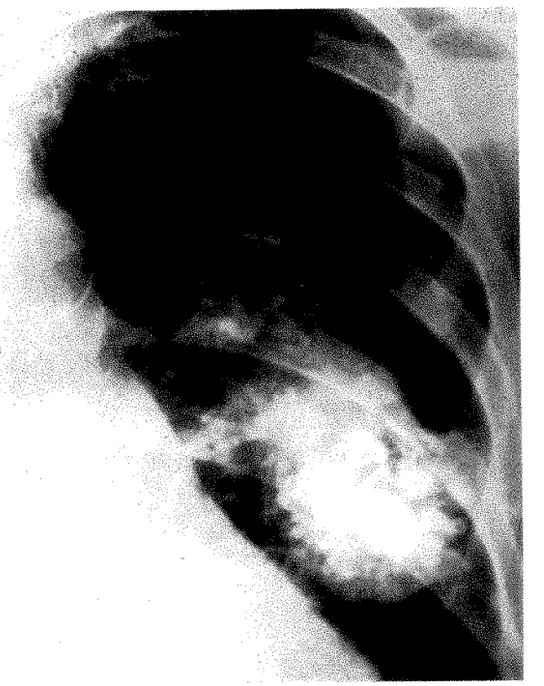


Fig. 4. Thick-walled "eggshell" calcifications inside a mass are characteristic of PMF.

fungus infections. Their presence outside a mass may confirm the history of silica exposure, but is not necessarily helpful in the differential diagnosis between progressive massive fibrosis and carcinoma. Occasionally, "thick eggshells" or almost solid chunks of calcium are found inside a mass caused by PMF. This virtually excludes a primary lung cancer (Fig. 4). This type of calcification may resemble that of a hamartoma, but the shape and density of the mass will usually differentiate between the 2 lesions.

The small nodules in the lungs of patients who have had silica exposure, either from pure silica or from the mixed dust in coal mines, tend to calcify. In older coal miners, particularly the anthracite workers, there is calcification in at least a few of the nodules in up to 10 per cent of patients. The calcification starts as a central dot, thus helping to differentiate it from the diffuse calcification that occurs in the nodules of histoplasmosis. Some masses caused ay PMF contain these small calcifications, b feature which is most helpful in differentiating the lesion from a carcinoma (Fig. 5).

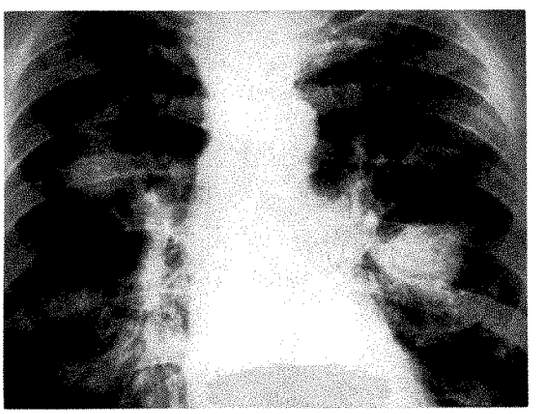


Fig. 3. PMF plus carcinoma. The squamous cell carcinoma in the left lung is relatively dense because it is almost spherical. The mass of PMF in the right lung is relatively radiolucent because it is flat.

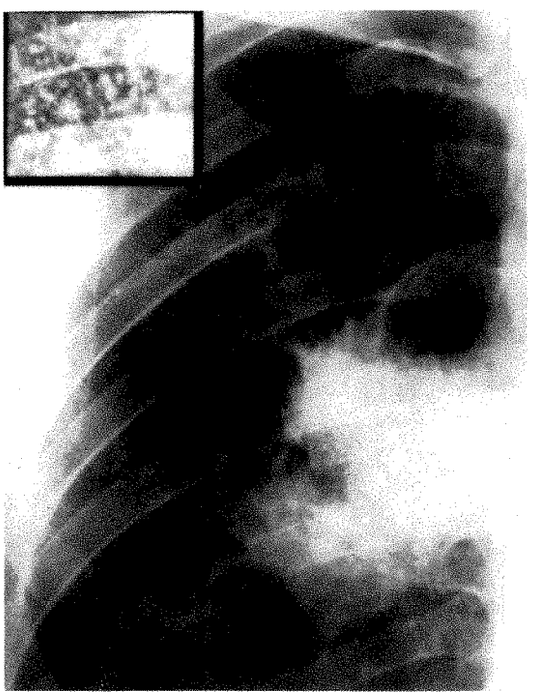


Fig. 5. The small nodules in silicosis and anthrasilicosis tend to calcify, beginning as a central dot (insert). Their presence in the hilar mass helps establish diagnosis of PMF, even though there are no small nodules elsewhere in the lungs.

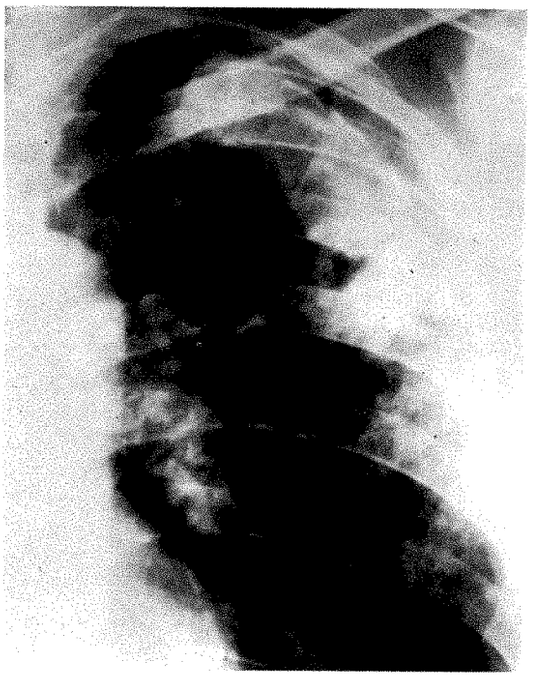


Fig. 6. Linear calcifications along the peripheral margin of PMF are characteristic but rare.

Extensive calcification of small nodules is much more common in patients who quit the mines many years previously than it is in current miners.

Linear calcifications occasionally occur along the border of PMF. They have always been in the lateral margin of the mass and have been seen in both hard and soft coal miners (Fig. 6). This type of calcification does not appear to have been described in a carcinoma.

Some patients have more than one type of calcification. It is not clear why calcium is deposited in the nodules and masses of some miners but not in others. The incidence of calcification appears to be somewhat proportional to the amount of silica in the lungs and is thus more common in the miners of anthracite coal and higher rank soft coal.

Satellite Nodules. The presence of multiple small nodules near a lung mass favors pneumoconiosis or infection, rather than carcinoma, even when there are no nodules elsewhere in the lungs. Satellite nodules are rare in carcinoma.[2] Their presence strongly suggests PMF if the tuberculin skin test is negative (Fig. 7).

Course of PMF. Previous roentgenograms to determine the evolution of a lung mass are most helpful and may be virtually diagnostic of PMF if: (1) the mass has been formed by the coalescence of nodules, rather than by growth of a single nodule; (2) the mass has decreased in size over a period of time; (3) the margin of the mass has become more sharply defined; or (4) the mass has migrated toward the hilum.

Indeterminate Lesions

PMF typically starts in the periphery of the lung. If it remains there, its contour is likely to be diagnostic. Unfortunately, in some cases, the mass migrates medially and may reach the hilum or mediastinum over a period of 10 or more years. It may then closely resemble a malignancy (Fig. 8). During this medial migration, the mass may assume a somewhat spherical shape with an irregular margin which cannot be differentiated from carcinoma in the absence of previous roentgenograms (Fig. 9, *A* and *B*). A complete occupational history is important because the small nodules of coal workers' pneumoconiosis may disappear after termination of dust exposure, while PMF may be progressive. Thus, the confusing roentgenographic finding of PMF without small nodules is more likely to



Fig. 7. Satellite nodules near a mass of PMF. Satellite nodules strongly favor pneumoconiosis or infection, even when there are no nodules elsewhere in the lungs. They are rare in carcinoma.

occur in a former miner than in a current miner.

Tomography has been of little value in the differential diagnosis except to show satellite nodules. The presence of an air bronchogram in the lesion favors PMF over squamous cell carcinoma, but is not evidence against a bronchioloalveolar carcinoma. Unfortunately, in most old lesions of PMF, no air bronchogram is seen in the center of the lesion. A brush biopsy is helpful only if positive for malignancy or tuberculosis. We believe that this technique is most likely to be of value in cavitated lesions when the sputum is negative. However, as the incidence of tuberculosis decreases in the general population, there has been a comparable decrease in its incidence among coal workers. We did not find evidence of tuberculosis in any of the above cases.

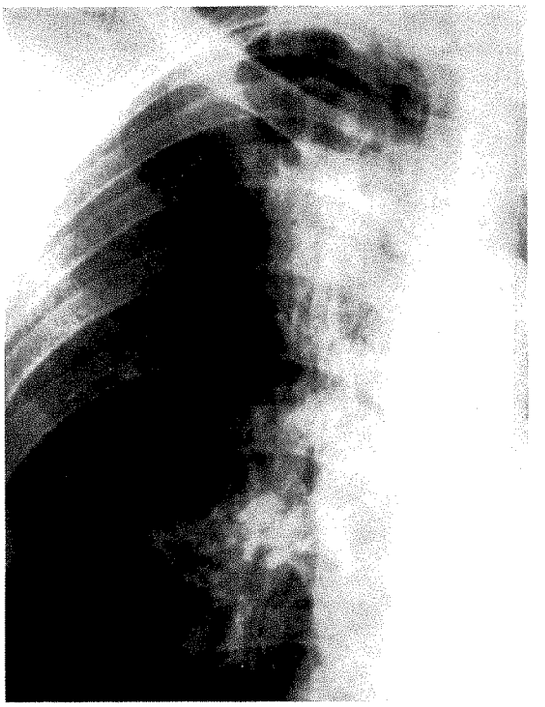


Fig. 8. Paramediastinal PMF. Although PMF usually starts at the periphery of the lung, it often migrates centrally where it may closely simulate a carcinoma.

SUMMARY

Coal miners with at least 15 years of dust exposure may have a solitary density caused by progressive massive fibrosis (PMF), even when there is little or no nodularity elsewhere in the lungs. The mass may closely resemble a carcinoma, but the correct diagnosis can be made if the typical roentgen features of PMF are present. The characteristic findings are as follows:

1. The lateral border of the mass is flat, often elongated, and parallels the rib cage.

2. The mass is thin in the lateral or oblique projection and is more radiolucent in the frontal projection than a spherical lesion.

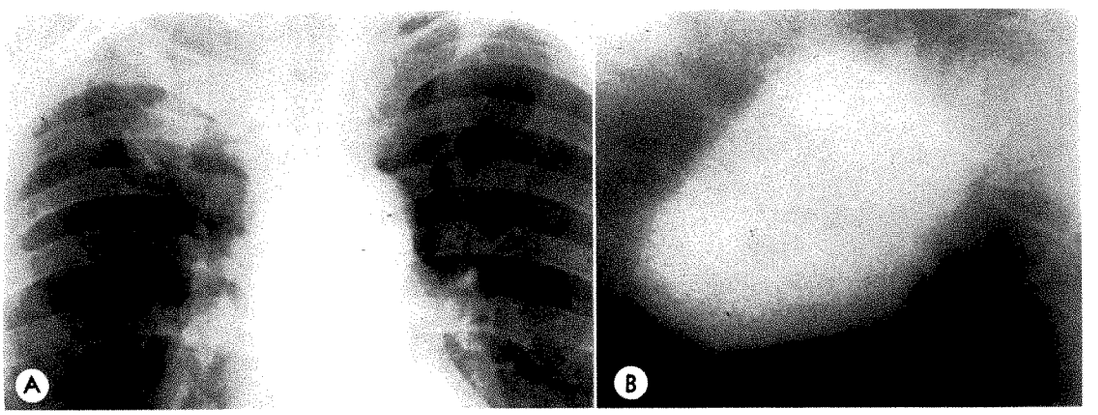


Fig. 9. (*A*) PMF without small nodules in a patient who quit the mines 37 years previously. During medial migration, the mass has become spherical and resembles a carcinoma. (*B*) Tomogram. The spiculated margin of this PMF exactly simulates a carcinoma.

3. Characteristic calcifications are present.

4. There are multiple satellite nodules near the mass.

Previous roentgenograms are most helpful and may be virtually diagnostic, if there is evidence that the mass developed by the coalescence of nodules, if the mass decreased in size, if its margin became more sharply defined or if the mass migrated medially.

Careful evaluation of the lung mass according to the above criteria will help prevent unnecessary surgery in this poor risk group.

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Vol. 117, No. 4

A PHANTOM FOR THE EVALUATION OF TECHNIQUES AND EQUIPMENT USED FOR ROENTGENOGRAPHY OF THE CHEST*

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PUBLIC Law 91–173 passed by the Congress in 1969 and often referred to as the "black lung law" established provisions for roentgenographic examinations of approximately 100,000 active coal miners. These examinations were to be carried out in approved facilities of which there are presently about 270. If there is to be any uniformity of roentgenographic quality, some test object that can be sent to these facilities is needed. It seems reasonable to assume that as such programs move into other areas of industrial medicine, there will be a sustained need for some means of evaluating roentgenologic procedures used in such studies. Surely, there must be some common denominator for roentgenographic quality if any long-time, generalized effects are to be reported for epidemiologic purposes.

A roentgenogram of less than good quality may be usable for a single, local determination made by a single physician. It is not adequate for a mass study where current findings are to be reported by a number of readers. It is even less acceptable for inclusion in a system subject to periodic review over a period of years.

Test objects for purposes such as that considered here have great value. Patients are not suitable, for it is virtually impossible to select at each facility a patient having common characteristics. Then, too, there is always the charge that such patients are receiving unproductive exposure. In addition, a reproducible test object can be used over a period of years to evaluate and incorporate new technology and new materials since the original conditions can always be reproduced at any time and at any location.

Since aluminum test blocks have been widely used, first thoughts naturally are given to that material. For many applications, one would like to use a material providing scattering comparable to that of tissue, but aluminum does not meet this requirement. Water or some of the tissue equivalent materials could be used. A stepped water phantom would involve a complicated container. The tissue equivalent plastics are sometimes difficult to obtain and are not inexpensive. For that reason, a readily available plastic with scattering characteristics not too different from tissue was selected.

DEVISE OF TEST PHANTOM

The test phantom that we have devised consists of 10 sheets of $\frac{3}{4}$ inch cast thermoplastic acrylic resin, Plexiglas-G. The Plexiglas-G that we have used has what the manufacturer calls Class A tolerance +0.030 inches, −0.080 inches and a nominal weight of 4.62 pounds per square foot. The sheets are 6 inches wide and, since each step is $1\frac{1}{2}$ inches long, the total length is 15 inches. When the phantom is exposed employing the factors routinely used for a chest patient measuring 20–22 cm., the phantom provides the range of film densities found in a chest roentgenogram. A readout of the densities of the steps can be plotted against the step number to provide a graph that can be compared with another graph made under known and controlled conditions. Such a comparison provides information indicative of processing

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
The work upon which this publication is based was performed pursuant to Contract FDA 72-314 with the Bureau of Radiological Health, Public Health Service, Food and Drug Administration, and the National Institute for Occupational Safety and Health, Department of Health, Education and Welfare.

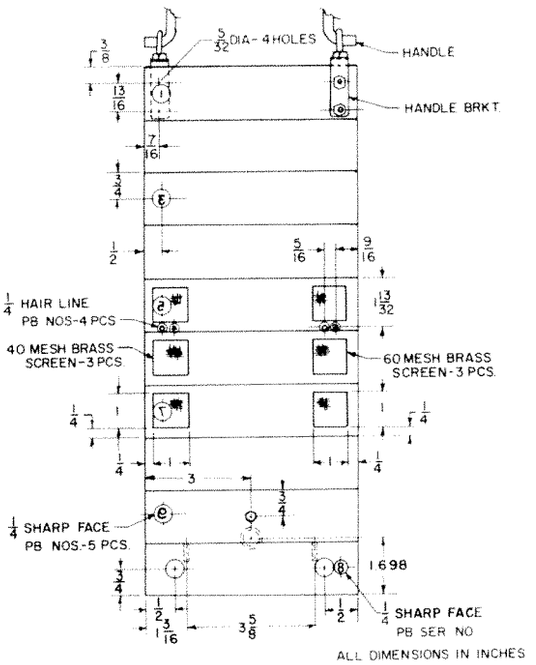


FIG. 1. Drawing of phantom, front view.

procedures as well as exposure factors.

One of the major problems in the "black lung" program lies in the fact that many of the facilities involved are used for general roentgenography. As a result, the geometry that results from re-positioning the tube leads to some pretty terrible geometry due to the fact that rigid stops, markers, etc., have never been provided. To get an evaluation of the geometry used, a lead pin is embedded in the top of the phantom and a ring is embedded in the bottom of the thickest step. The positions of the pin and ring are such that a 72 inch source film distance and with 1 inch space between the film and the face of the cassette holder, the image of the pin will be centered in the ring if the source is centered to the film and at right

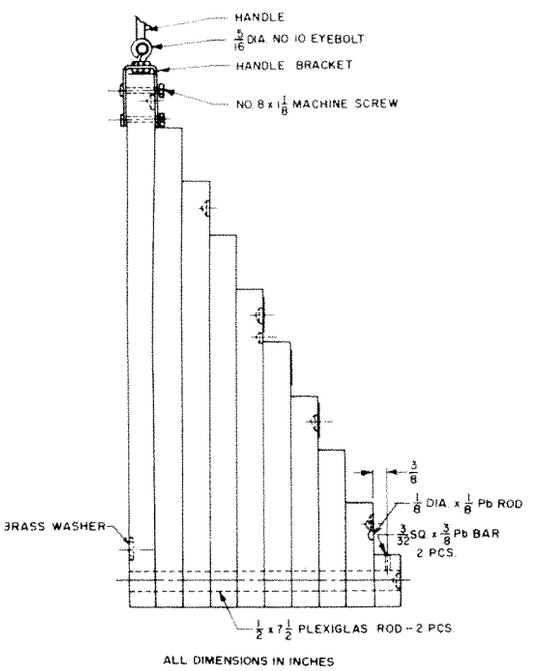


FIG. 2. Drawing of phantom, side view.

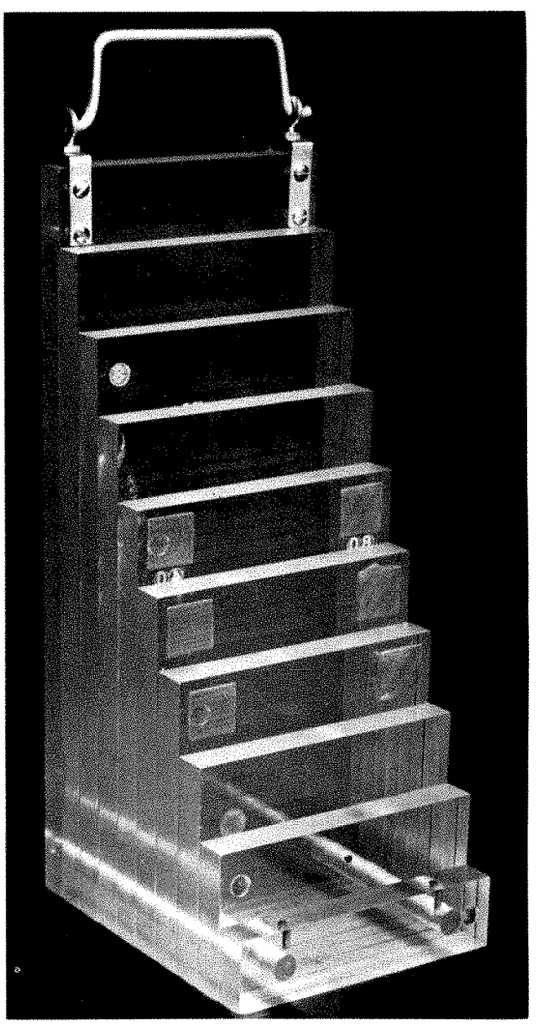


FIG. 3. Photograph of phantom.

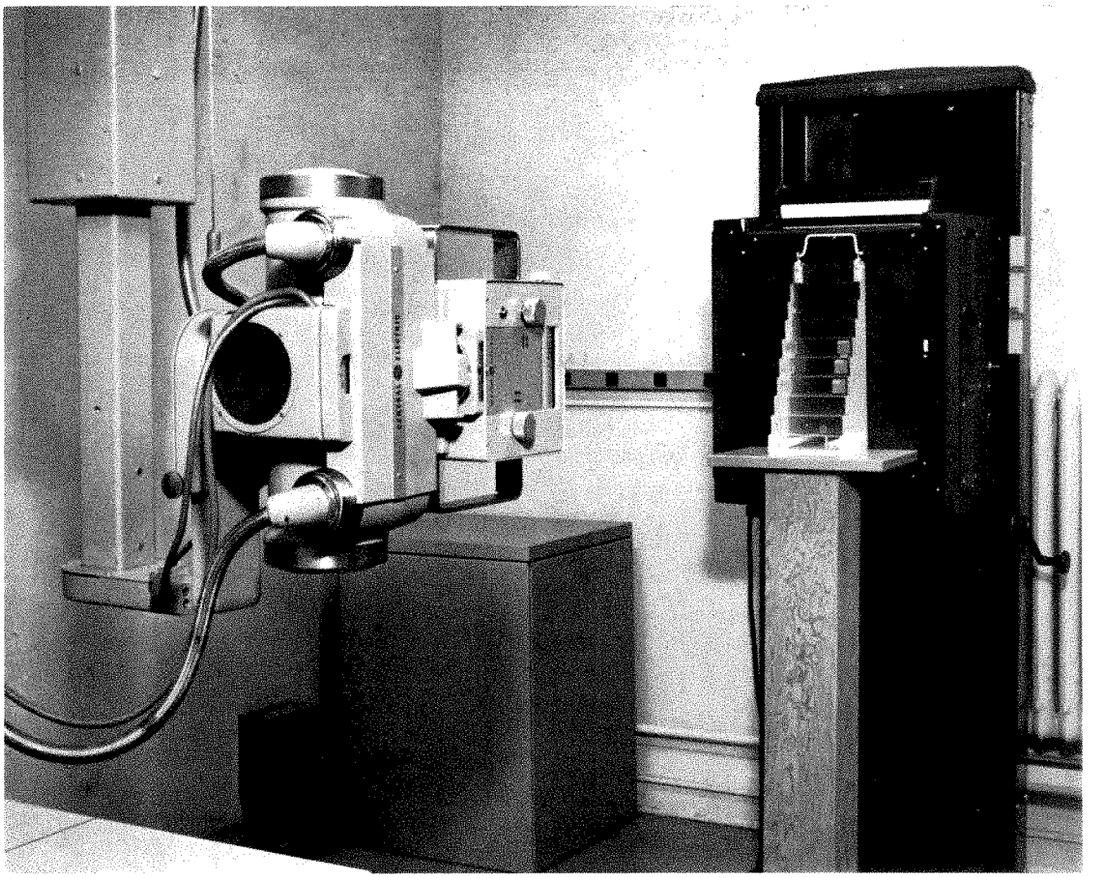


FIG. 4. Photograph of phantom and cassette holder.

angles in both planes. The use of correct geometry is very critical when grids are used, especially a grid of high ratio.

In facilities where equipment is of limited capacity, there may be a tendency to cheat on the required 72 inch source-film distance. In the top of the thickest step are 2 lead bars, 3/32 inch square and 3/8 inch long. When a 72 inch distance is used the spacing between the inner images of the

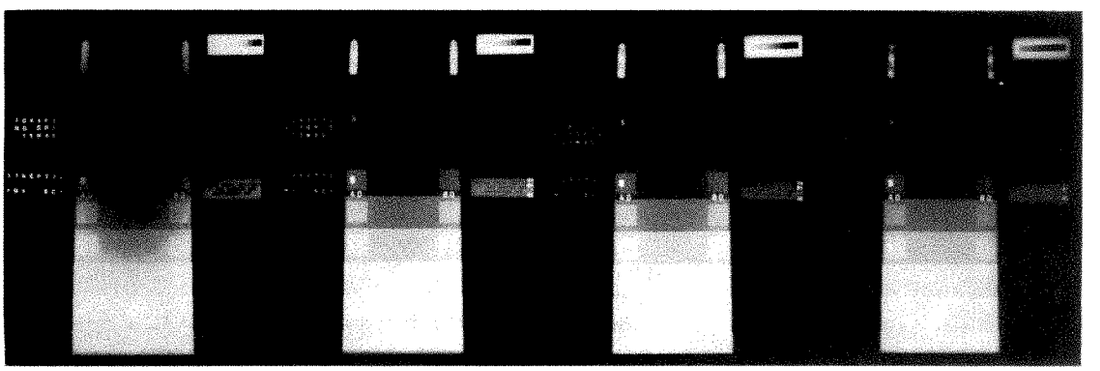


FIG. 5. Roentgenograms of phantom: 70 kVp, 15 mAs, no grid; 100 kVp, 10 mAs, 6:1 grid; 115 kVp, 7.5 mAs, 8:1 grid; 130 kVp, 5 mAs, 10:1 grid.

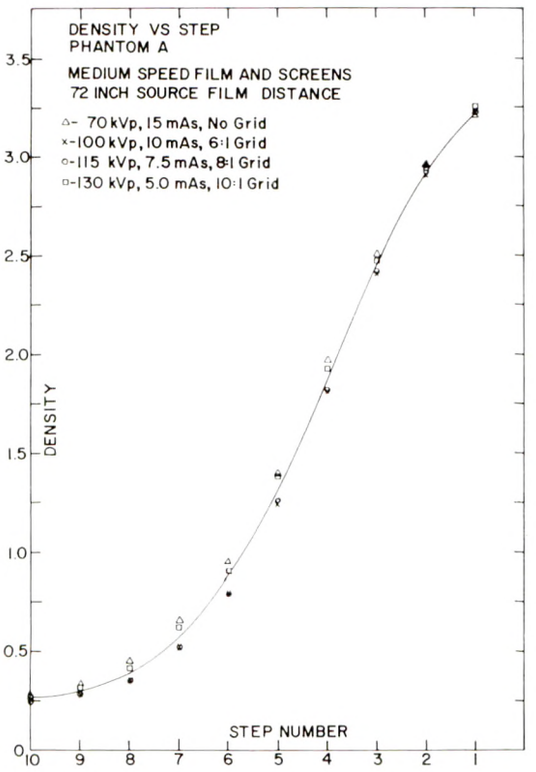


Fig. 6. Density *vs.* step number for phantom roentgenograms.

bars is 10 cm. A measurement of this distance can be used to confirm compliance and if necessary to calculate the actual distance used.

To record gross lack of roentgenographic detail usually associated with poor screen contact, pieces of brass wire mesh of 40 and 60 mesh are mounted on steps 5, 6 and 7. No great significance is attached to their use for other than detection of a gross condition such as poor screen contact or movement of some mechanical structure during exposure.

Since the phantom weighs 15 pounds and has a very smooth surface, a hinged handle has been provided.

Figures 1 and 2 provide information as to construction and dimensions. Figure 3 is a close up photograph and Figure 4 shows the phantom in place in front of a cassette holder.

The Plexiglas-G sheets have lengths of $1\frac{1}{2}$, 3, $4\frac{1}{2}$, 6, $7\frac{1}{2}$, 9, $10\frac{1}{2}$, 12, $13\frac{1}{2}$, and 15 inches. The $\frac{1}{4}$ inch sharp face lead numbers for step identification and serial number and the $\frac{1}{4}$ inch hair line lead numbers for brass mesh identification are placed in holes drilled in the Plexiglas and the holes filled with a clear polyester casting resin. The 2 lead bars, the lead pin and the ring are also placed in holes drilled in the Plexiglas and embedded in clear polyester casting resin. The brass wire mesh is placed on the surface of the Plexiglas and held in place by a thin coat of the casting resin. After all parts have been assembled on or in the Plexiglas, the sheets are assembled and clamped in place, and a small amount of Plexiglas solvent cement (dichloroethane) is placed along the junction of each of the sheets.

EXPERIMENTAL STUDIES

In addition to providing a fast and simple evaluation of a facility, the phantom is useful for experimental studies.

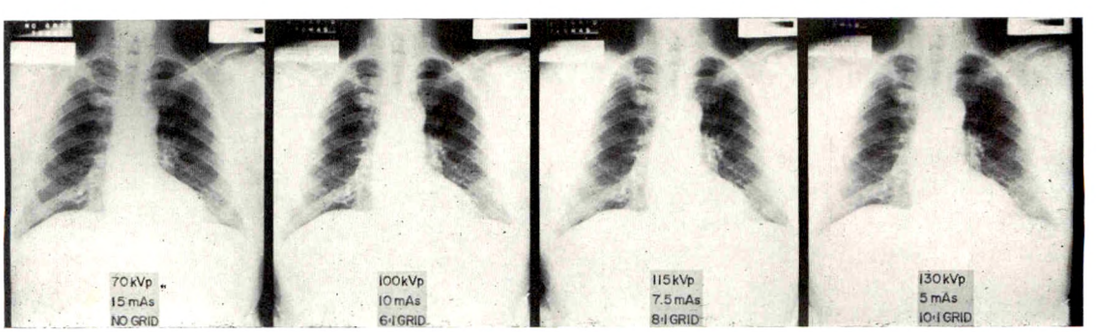


Fig. 7. Chest roentgenograms: 70 kVp, 15 mAs, no grid; 100 kVp, 10 mAs, 6:1 grid; 115 kVp, 7.5 mAs, 8:1 grid; 130 kVp, 5 mAs, 10:1 grid.

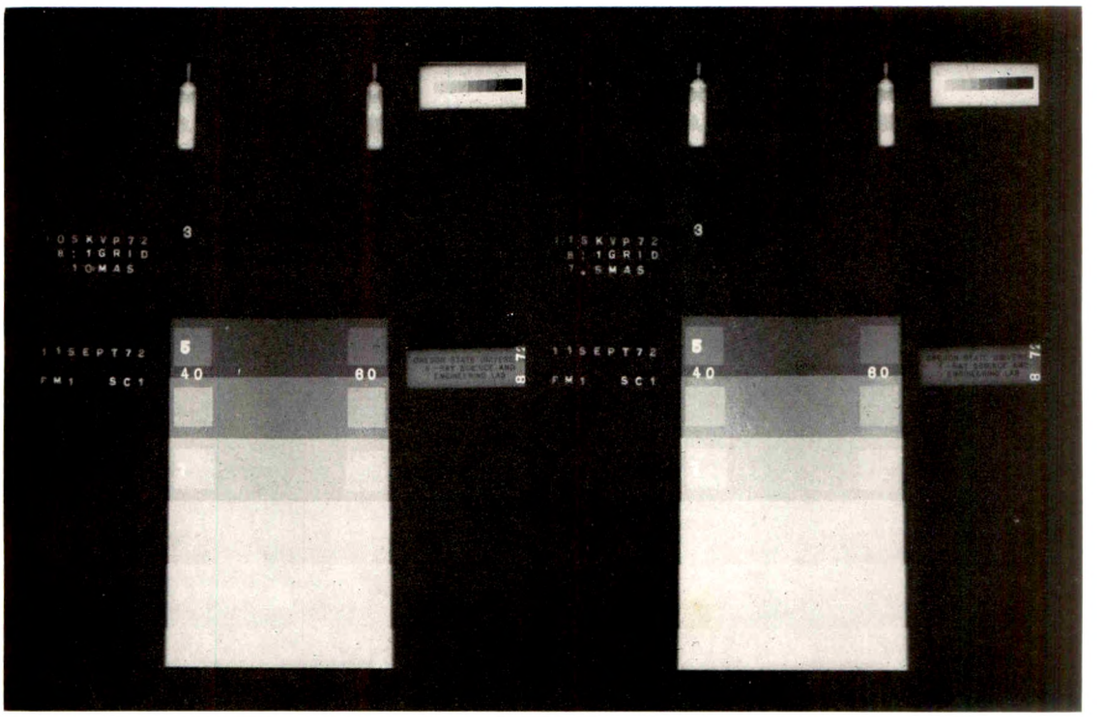


Fig. 8. Roentgenograms of phantom: 105 kVp, 10 mAs, 8:1 grid; 115 kVp, 7.5 mAs, 8:1 grid.

An example of one such study is that made on the use of grids of different ratios. There is, of course, general agreement that 100 line grids should be used. The agreement as to the value of a grid and the ratio to be used has been the subject of a great deal of discussion. The purpose of a grid is to reduce scattered radiation. There is a tendency in chest roentgenography when using a grid to increase kilovoltage in order to retain a short exposure time. If the kilovoltage is increased, the scattered radiation rate and energy increase, and, beyond a certain point, the contrast with a grid is less than would have been provided by a non-grid technique.

To develop some information on what this kilovoltage might be, we studied 100 line grids having ratios of 6:1, 8:1 and 10:1. The roentgenograms and techniques without a grid and with the 3 grids are shown in Figure 5. The exposure in milliampere-seconds lies within the ranges generally found in use with single-phase equipment. It will be seen that roentgenograms using 70 kVp without grid are comparable with those using a grid when 100 kVp is used with a 6:1 grid, 115 kVp when an 8:1 grid is used and 130 kVp when a 10:1 grid is used.

When the roentgenographic density of the steps is plotted against the step number (*i.e.*, thickness) as shown in Figure 6, it will be seen that there is good agreement. Figure 7 shows roentgenograms made on the same individual using the techniques employed with the phantom. Again it will be seen that the results are comparable. It seems reasonable to assume that grids of any ratio can be used to produce acceptable results if the kilovoltage is adjusted for the grid ratio.

In the examples shown, the contrast is comparable with that obtained without grid. If contrast is to be increased through the use of a grid, some lower kilovoltage with an increase in milliampere-seconds must be used. To illustrate this, Figure 8 shows for comparison a roentgenogram made using an 8:1 grid at 115 kVp and 7.5

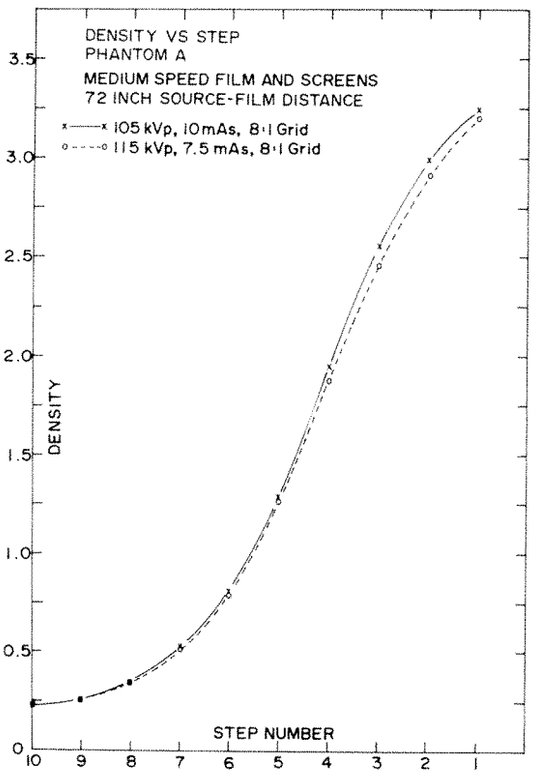


Fig. 9. Density *vs.* step number for phantom roentgenograms.

milliampere-seconds and a roentgenogram made with the same grid reducing the kilovoltage to 105 kVp and increasing the exposure to 10 milliampere-seconds. As would be expected, the reduction in kilovoltage leads to an increase in contrast as shown in Figure 9, where density is plotted as a function of step number. There is, of course, a slight reduction in latitude. Figure 10 shows roentgenograms made on the same individual using the techniques employed with the phantom.

Similar studies are currently underway using three-phase, 12 pulse and battery powered equipment.

SUMMARY

A test phantom that is useful for evaluation of procedures in chest roentgenography has been made. It is not expensive, the materials are generally available and its use to evaluate a technique or a facility is not complicated.

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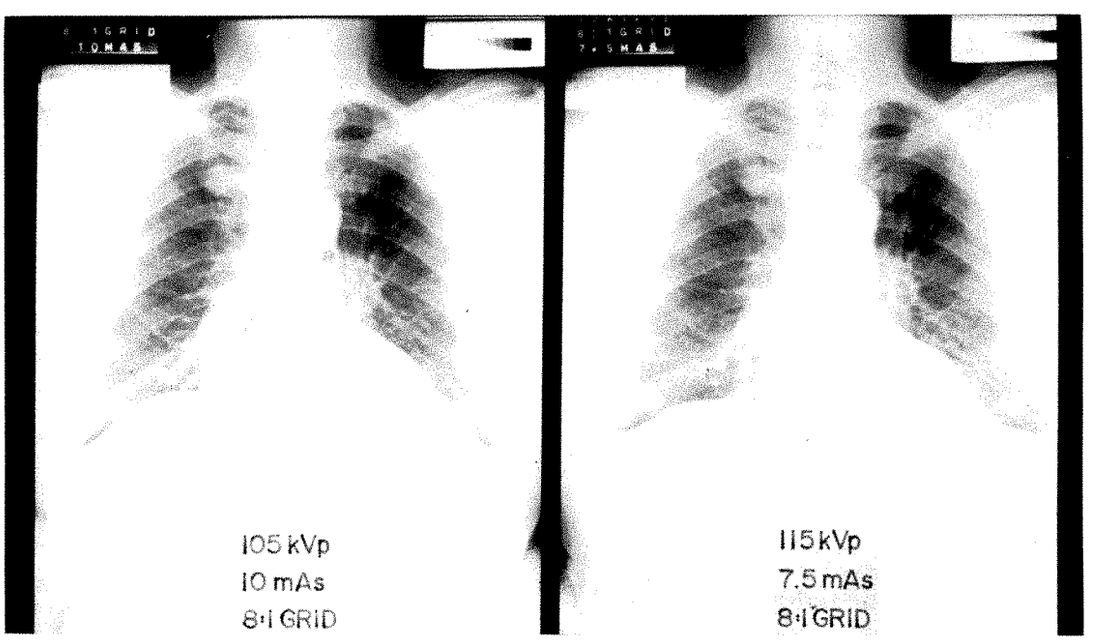


Fig. 10. Chest roentgenograms: 105 kVp, 10 mAs, 8:1 grid; 115 kVp, 7.5 mAs, 8:1 grid.

VOL. 117, NO. 4

PULMONARY SARCOIDOSIS*

ROENTGENOLOGIC ANALYSIS OF 150 PATIENTS

By DONALD R. KIRKS, M.D., VINCENT D. McCORMICK, M.D., *and* RICHARD H. GREENSPAN, M.D.
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SARCOIDOSIS is a systemic granulomatous disease of unknown etiology. Diagnosis should be considered established in patients with consistent clinical features and biopsy evidence of epithelioid tubercles or a positive Kveim test.[4] The typical histologic appearance of tubercles with little or no necrosis is not in itself diagnostic, and tuberculosis, fungal infections, certain pneumoconioses, as well as numerous other causes of a local sarcoid reaction must be excluded.

The roentgenologic manifestations of pulmonary sarcoidosis were initially described more than 25 years ago.[2,11,19] Since that time, numerous articles have been written concerning clinical findings and natural history,[1,16,17,21–23] effects of steroid therapy,[24] the roentgenographic course of the disease,[5,20] and its complications.[10]

Both bilateral hilar lymphadenopathy and bilateral hilar with right paratracheal lymphadenopathy have been described as classic roentgenologic findings.[11,25] Nodular, linear, or mixed pulmonary densities—sparing the bases and apices—are considered the typical roentgenographic findings of pulmonary parenchymal disease.[10] The observation in numerous patients of bilateral paratracheal lymphadenopathy and of pleural effusion prompted this retrospective study. Also, the frequency of various roentgenographic parenchymal patterns in patients with pulmonary sarcoidosis has not been previously documented.[9,12]

MATERIAL AND METHOD

This study included patients from San Francisco General Hospital, Veterans Administration Hospital in San Francisco, and the University of California Hospitals at San Francisco. The clinical charts and chest roentgenograms of 162 patients with a tissue or Kveim biopsy diagnosis of sarcoidosis were reviewed. The period of follow-up ranged from 3 months to 18 years. At least 2, and often 3, observers reviewed the roentgenograms.

RESULTS

Abnormalities of the chest were noted in the roentgenograms of 150 (93 per cent) of the 162 patients. The 188 positive tissue diagnoses obtained from their records were further detailed according to site of involvement (Table I). Sixty-three per cent of the patients were Negro (Table II). Negro females outnumbered Negro males 2 to 1, while Caucasian females outnumbered Caucasian males only 1½ to 1. Seventy-two per cent of the patients were in their 20s or 30s at the time of tissue diagnosis.

Forty-three per cent of the patients showed only lymph node enlargement on the initial chest roentgenogram (Table III). Forty-one per cent had both lymphadenopathy and parenchymal disease; 16 per cent showed only parenchymal abnormality.

LYMPH NODE ABNORMALITIES

One hundred and twenty-six (84 per cent) of the patients in this series of 150 had lymphadenopathy. This type of lymphadenopathy was analyzed as to exact location at the time of maximal enlargement (Table IV). Ninety per cent of the patients with lymphadenopathy showed 1 of 3 abnormalities: bilateral hilar lymphadenopathy; bilateral hilar and bilateral para-

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TABLE I

POSITIVE TISSUE DIAGNOSES FOR SARCOIDOSIS IN 150 PATIENTS WITH ROENTGENOGRAPHIC CHEST ABNORMALITIES

Tissue	No. of Patients
Scalene lymph node	69
Liver	50
Lung	18
Mediastinal lymph node	13
Skin	11
Kveim reaction	7
Conjunctiva	4
Cervical lymph node	3
Muscle	3
Pleura	3
Lacrimal gland	2
Bronchus	1
Kidney	1
Epididymis	1
Epitrochlear lymph node	1
Parotid gland	1

tracheal lymphadenopathy; or bilateral hilar and right paratracheal lymphadenopathy. Bilateral hilar lymphadenopathy alone and bilateral hilar with bilateral paratracheal lymphadenopathy (Fig. 1*A*; 4; and 6, *A* and *B*) occurred in an equal number of cases. No correlation could be established between race and incidence of bilateral hilar enlargement. There was, however, a predilection for bilateral hilar and bilateral paratracheal lymphadenopathy in the Caucasian patient (Table IV). Bilateral hilar with right paratracheal lymphadenopathy occurred slightly less frequently and was more common in Negroes than in Caucasians. The remaining patients in this group showed other types of lymph node abnormality. These abnormalities included bilateral paratracheal lymphadenopathy alone (2 patients), bilateral hilar and left paratracheal lymphadenopathy (9 patients), and unilateral hilar lymphadenopathy (1 patient). There was no instance of anterior mediastinal lymphadenopathy.

TABLE II

CLINICAL DATA OF 150 PATIENTS WITH ROENTGENOGRAPHIC CHEST ABNORMALITIES

		No. of Patients
Negro		94(62.7%)
Female	62(41.3%)	
Male	32(21.4%)	
Caucasian		56(37.3%)
Female	33(22.0%)	
Male	23(15.3%)	
Age at Diagnosis		
0– 9 years		0
10–19 years		14(9.4%)
20–29 years		75(50.0%)
30–39 years		33(22.0%)
40–49 years		18(12.0%)
50–59 years		8(5.3%)
60–69 years		2(1.3%)

PARENCHYMAL ABNORMALITIES

Parenchymal abnormalities (Table IV) were noted in 95 patients (63 per cent) during the course of follow-up. Most patients developed more than 1 pattern of pulmonary involvement (average of 1.7 parenchymal patterns per patient).

A reticulonodular pattern was the most common parenchymal abnormality. This group included pure nodular, pure reticular, and mixed reticulonodular densities. The mixed reticulonodular pattern consisted of fine linear densities and small nodules measuring approximately 3 to 5 mm. in diameter (Fig. 2; 3*A*; and 7*A*); it was observed in 70 patients. A pure miliary pattern was included in this group but was seen in only 2 patients. A pure linear pat-

TABLE III

CHEST ABNORMALITIES IN 150 PATIENTS, AS SEEN ON THE INITIAL ROENTGENOGRAM

		No. of Patients
Lymph node abnormality only		65(43.3%)
Negro	40(26.6%)	
Caucasian	25(16.7%)	
Lymph node and parenchymal abnormalities		61(40.7%)
Negro	41(27.3%)	
Caucasian	20(13.4%)	
Parenchymal abnormality only		24(16.0%)
Negro	13(8.7%)	
Caucasian	11(7.3%)	

TABLE IV

ABNORMALITIES SEEN ON CHEST ROENTGENOGRAMS OF 150 PATIENTS WITH PULMONARY SARCOIDOSIS

Abnormalities	Negro	Caucasian	Total
Lymph node enlargement	81 (81 patients)	45 (45 patients)	126 (126 patients)
bilateral hilar	27	12	39
bilateral hilar and bilateral paratracheal	20	19	39
bilateral hilar and right paratracheal	28	8	36
other	6	6	12
Parenchymal abnormality	103 (60 patients)	54 (35 patients)	157 (95 patients)
reticulonodular	50	30	80
fibrotic	26	16	42
chronic acinar	24	8	32
large nodular	3	0	3
Other	15 (15 patients)	8 (8 patients)	23 (23 patients)
cardiomegaly (no other known cause)	4	3	7
pleural effusion (no other known cause)	3	2	5
calcified nodes	2	3	5
pneumothorax	4	0	4
lobar atelectasis	1	0	1
mycetoma	1	0	1

tern with central "honeycomb"[7] lucencies of 1 to 10 mm. (seen in 8 patients) was also included in this group.

Fibrosis was the next most common parenchymal pattern. Roentgenographic criteria for this diagnosis were linear pulmonary densities which persisted for long intervals of time and were associated with decrease in lung tissue—retraction and distortion of fissures, hili, vessels, bronchi, and mediastinal or other pleural surfaces.[5,6] These fibrotic parenchymal changes ranged from minimal linear scarring to more classic conglomerate densities of the upper lobe with associated hilar retraction and extensive bullous change (Fig. 7*B*).

A chronic acinar pattern noted during the course of disease comprised 20 per cent of the parenchymal abnormalities. This was more commonly observed in the Negro patient. The acinar pattern was characterized by some or all of the following: coalescence; segmental or lobar distribution; fluffy margins; air bronchograms; and acinar nodules.[8] Only patients with persistence of the acinar pattern for at least 3 months, in association with negative bacteriologic cultures, were included in this group. Large segmental consolidations (Fig. 3, *A* and *B*) and scattered, hazy consolidations with irregular borders (Fig. 4) were the most commonly noted abnormalities within this group. All patients had either lymph node enlargement or parenchymal disease when this acinar pattern was initially noted: 9 patients had associated lymph node enlargement; 18 patients had lymph node enlargement and another parenchymal pattern; and 5 patients had no lymph node enlargement, but some other associated parenchymal abnormality. A reticulonodular density was the most common parenchymal abnormality associated with the "acinar" pattern; (18 of the 32 patients). The large, conglomerate densities of the upper lobe (Fig. 7*B*), often seen in end-stage fibrosis, were not included in this chronic acinar group.

Chest roentgenograms showed eventual clearing (Fig. 3*B*) in 10 of the 32 patients with a chronic acinar pattern. Twelve chronic acinar consolidations persisted with

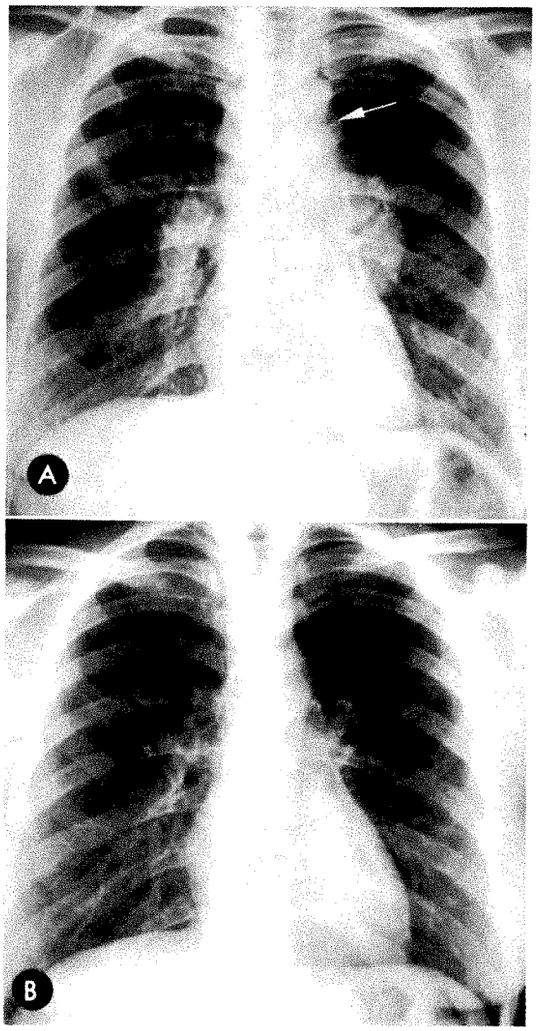


FIG. 1. (*A*) Bilateral hilar and bilateral paratracheal lymphadenopathy as seen on initial roentgenogram of the chest. Left paratracheal lymph nodes (arrow) are evident as a soft tissue density which silhouettes out the aortic arch. The pulmonary parenchyma is normal. (*B*) Follow-up roentgenogram 2 years later is normal. There is no evidence of lymphadenopathy and the aortic arch is clearly identified.

little change during the course of follow-up; an additional 10 patients developed fibrotic changes in the area of previous consolidation.

Only 3 patients (all Negro) showed a large nodular pattern. This consisted of sharply marginated nodular densities with an average diameter greater than 1 cm. scattered throughout the lung parenchyma (Fig. 5, *A–C*).

OTHER ABNORMALITIES

Cardiomegaly without any other known predisposing cause was observed in 7 patients (Table IV). Clinical records showed no electrocardiographic evidence of either arrhythmia or heart block. All of these patients had roentgenographic evidence of fibrotic pulmonary parenchymal disease.

A total of 8 instances of pleural effusion was found in the series of 150 patients. Three of these were associated with other diseases—congestive heart failure, tuberculosis, renal failure. Five patients had pleural effusion of no other known cause (Table IV). One of these 5 patients (Fig. 6, *A–C*) underwent a thoracotomy and open biopsy of both lung and pleura; pathologic changes were shown to be consistent with sarcoidosis, while numerous cultures of pleural fluid were negative. In 2 of the 5 patients, needle biopsies of the pleura showed noncaseating granulomas; cultures of the pleural fluid were negative. In these instances, the pleural fluid had the characteristics of an exudate. Two other patients had roentgenographic evidence of pleural fluid. Thoraco-

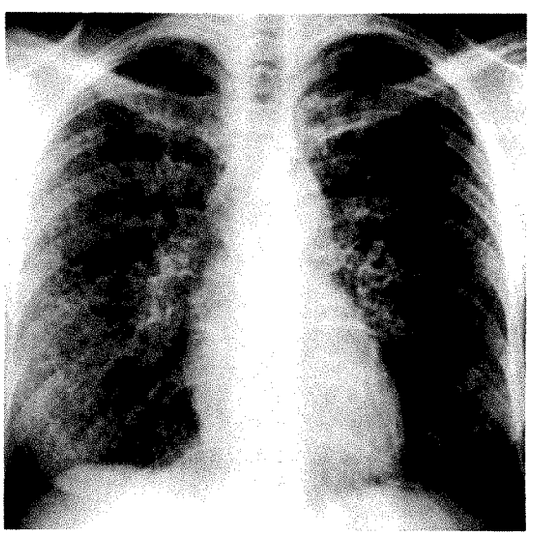


FIG. 2. Diffuse reticulonodular pulmonary parenchymal pattern without lymphadenopathy seen on chest roentgenogram.

centesis was not performed, but the pleural effusion subsequently resolved. Sputum cultures at the time of pleural effusion were sterile, and there was no clinical evidence of complicating illness. Three of the 5 patients, with no other known cause for pleural effusion than sarcoidosis, had associated pulmonary parenchymal disease. The other 2 had only hilar lymphadenopathy accompanying the pleural effusion.

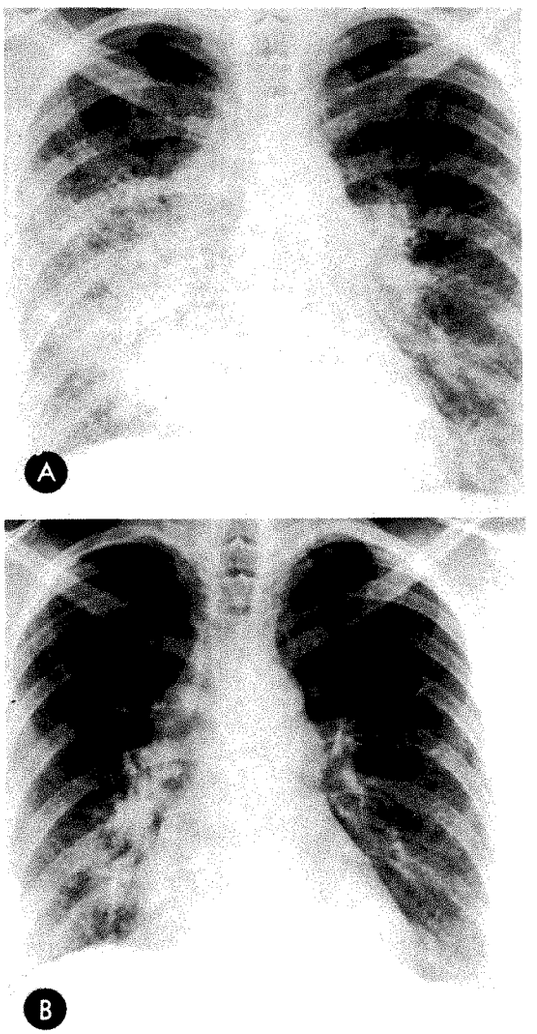


FIG. 3. (*A*) Diffuse reticulonodular parenchymal pattern seen on chest roentgenogram. There is also consolidation with air bronchograms involving the right middle and right lower lobes. (*B*) Roentgenogram taken 5 months later. There has been marked clearing of the pulmonary parenchymal disease and interval decrease in lymphadenopathy.

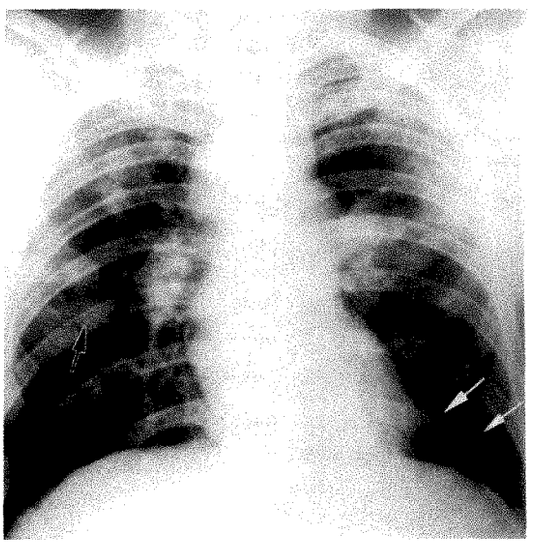


FIG. 4. Bilateral hilar and bilateral paratracheal lymphadenopathy as seen on chest roentgenogram. There are scattered areas of parenchymal consolidation with indistinct margins. Air bronchograms are noted (arrows) within several of these consolidations.

Although roentgenographic evidence of segmental volume loss, in association with either pleural effusion (Fig. 5, *A–C*) or chronic acinar consolidation, was seen in 6 patients, there was only 1 instance of lobar atelectasis. This was due to biopsy proven endobronchial sarcoidosis. Five instances of lymph node calcification (Fig. 7, *A* and *B*), not seen on the initial roentgenograms, developed during the course of follow-up. There were 4 instances of pneumothorax. All 4 of these were in Negro patients who had extensive pulmonary parenchymal disease. There was only 1 case of pathologically proved mycetoma. This developed in a patient with extensive fibrotic disease.

DISCUSSION

San Francisco has a population which is 13.4 per cent Negro.[26] Since this series showed almost twice as many Negroes as Caucasians with pulmonary sarcoidosis, the predilection of this disease for Negroes is confirmed. This racial distribution is considerably different, however, from that re-

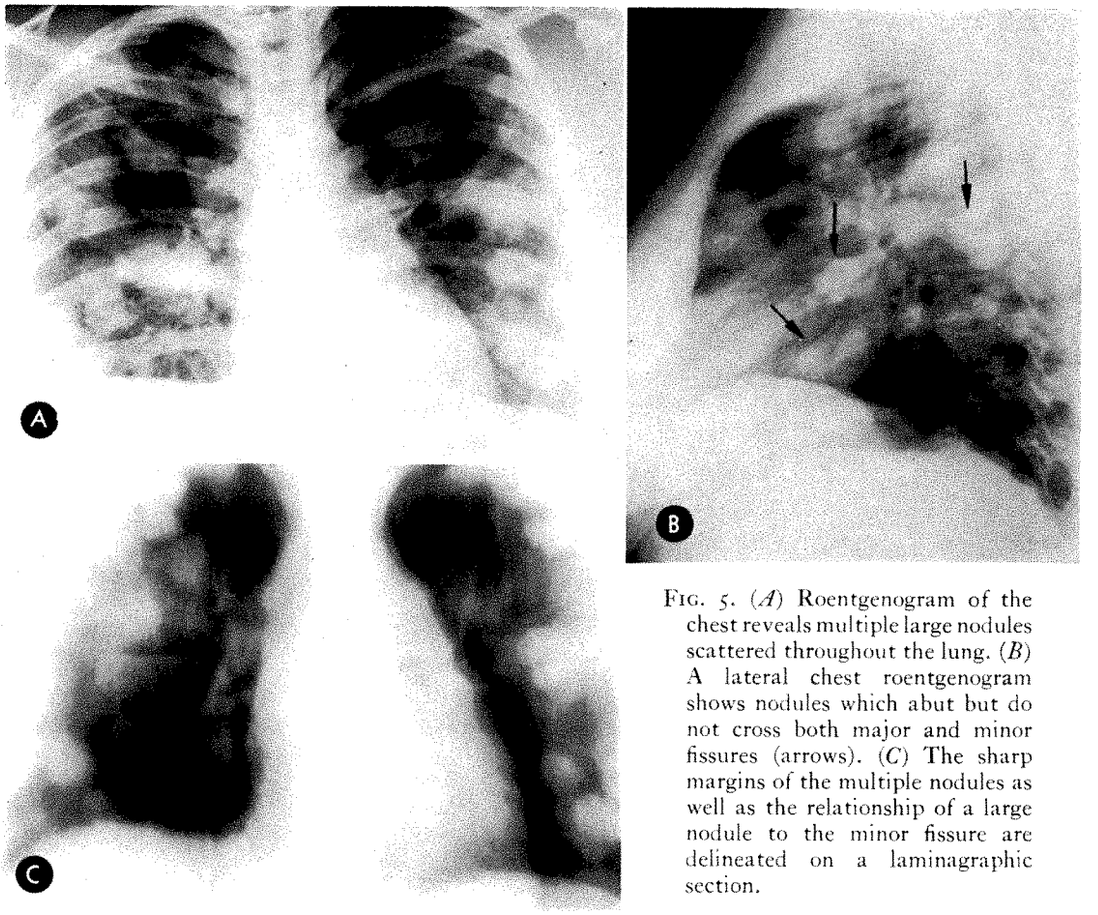


Fig. 5. (*A*) Roentgenogram of the chest reveals multiple large nodules scattered throughout the lung. (*B*) A lateral chest roentgenogram shows nodules which abut but do not cross both major and minor fissures (arrows). (*C*) The sharp margins of the multiple nodules as well as the relationship of a large nodule to the minor fissure are delineated on a laminagraphic section.

ported by Ellis and Renthal[5] (77 per cent Negro in 135 cases) and Freundlich *et al.*[10] (82 per cent Negro in 300 cases). Freundlich noted a higher incidence of right paratracheal lymphadenopathy, fibrotic contraction, cavitation, mycetoma formation, pneumothorax, and atelectasis in Negro patients. Bilateral hilar with bilateral paratracheal lymphadenopathy as well as nodal calcification occurred more frequently in Caucasians than expected according to the racial distribution of this study. There was a higher incidence of bilateral hilar and right paratracheal lymphadenopathy, chronic acinar parenchymal pattern, large nodular parenchymal disease, and pneumothorax in the Negro.

The frequency of the bilaterality of lymph node enlargement is noteworthy. This has been mentioned by other authors[9] but has been overshadowed by descriptions of the "1-2-3"[25] sign of bilateral hilar and right paratracheal lymphadenopathy. Bilateral hilar lymphadenopathy was present in 90 per cent of those patients with lymph node abnormality. Moreover, bilateral hilar with bilateral paratracheal lymphadenopathy was more common than bilateral hilar with right paratracheal lymphadenopathy. Left paratracheal lymphadenopathy was difficult to appreciate because of partial superimposition of the manubrium and aortic arch. In several of our patients, left paratracheal lymphadenopathy (Fig. 1, *A* and *B*) was apparent when roentgenograms showing maximal lymph node enlargement were compared to roentgenograms made after lymph node regression. An inability to visualize the superior margin of the aortic knob should raise the possibility of

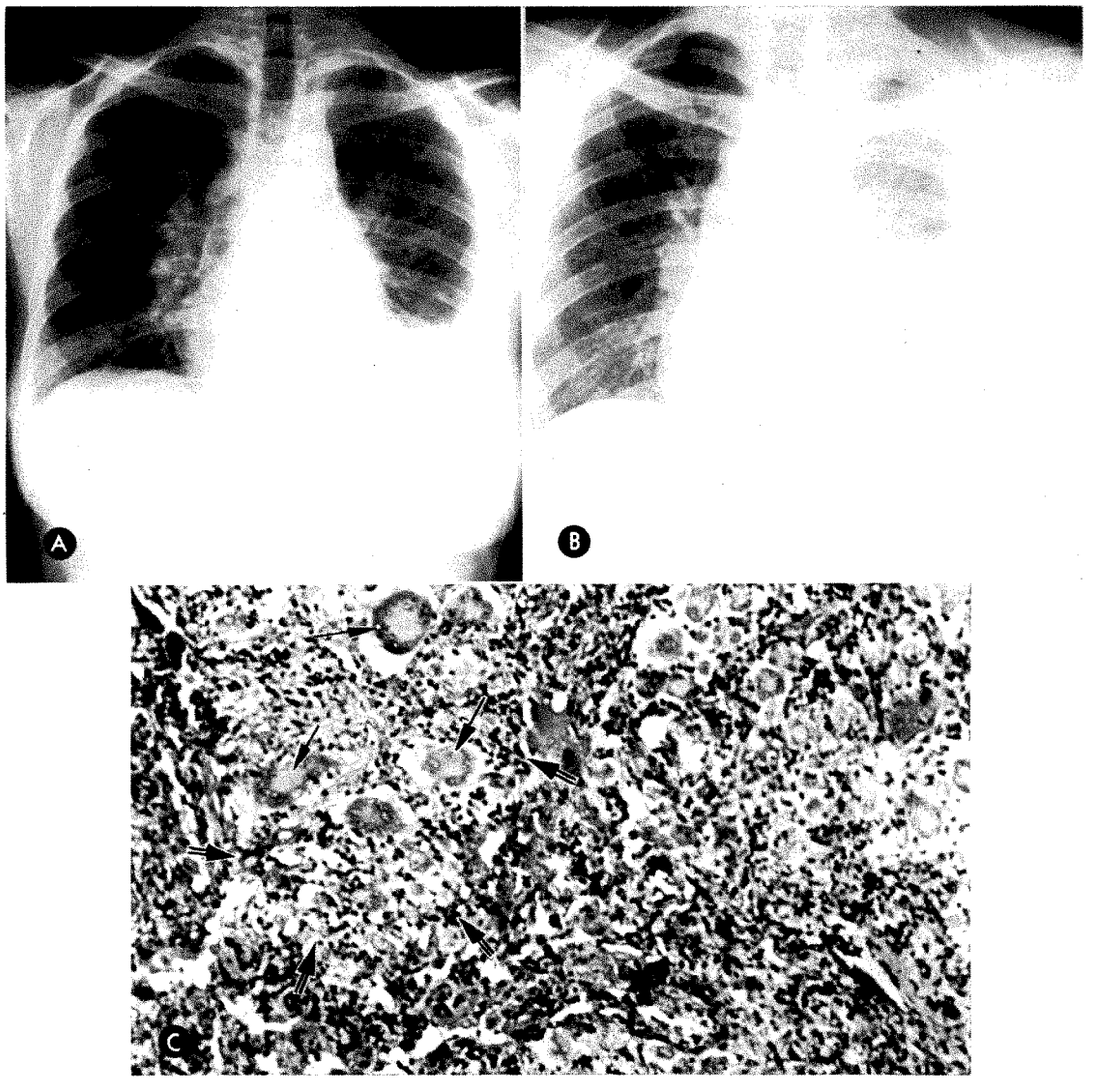


Fig. 6. (*A*) Bilateral hilar lymphadenopathy, bilateral paratracheal lymphadenopathy—left greater than right—and a large left pleural effusion as seen on initial roentgenogram. There is volume loss in the left lower lobe. (*B*) On a chest roentgenogram made 1 year later, interval increase in left pleural effusion can be seen. In this 1 year interim, there had been numerous thoracocenteses. The pleural fluid had the chemical characteristics of an exudate and all cultures were sterile. (*C*) Tissue taken during open lung biopsy shows noncaseating granulomas (large arrows) containing numerous giant cells (small arrows).

left paratracheal lymphadenopathy. Laminagraphy frequently confirmed the presence of left paratracheal lymphadenopathy. Paratracheal lymphadenopathy was frequently asymmetric. The occurrence of unilateral hilar[13,14] or anterior mediastinal lymphadenopathy was so rare that either of these would suggest some other diagnosis than sarcoidosis.

A reticulonodular pattern was the most commonly observed pulmonary parenchymal abnormality. This pattern has been described[25] as due to granulomatous nodules and associated fibrosis within the interstitium. Since this pattern can clear completely, the linear component probably represents an interstitial infiltrate rather than irreversible fibrosis. These reticulonodular

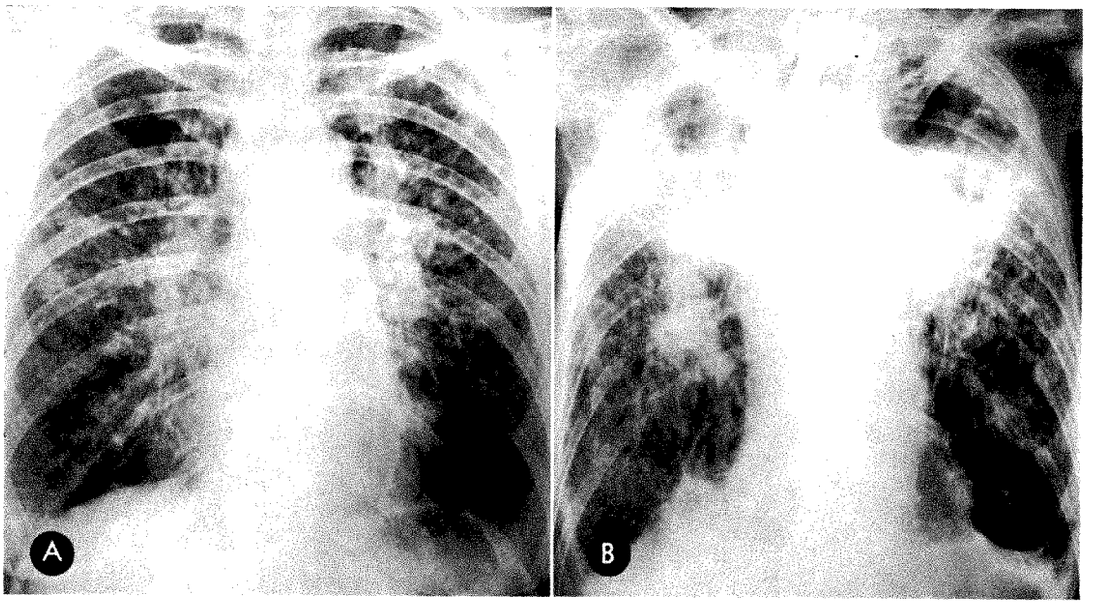


Fig. 7. (*A*) Bilateral hilar lymphadenopathy, right paratracheal lymphadenopathy, and diffuse reticulonodular pulmonary parenchymal disease as seen on initial chest roentgenogram. There was no history of occupational exposure to dust. (*B*) Follow-up roentgenogram shows a tube in place after tracheostomy was performed. There is extensive fibrosis with hilar retraction, upper lobe conglomerate densities, bullae, and diaphragmatic tenting. Bilateral pleural effusions are seen. Extensive nodal "eggshell" calcifications have developed within the chest and abdomen. At the time of autopsy, histologic examination of the lymph nodes revealed numerous noncaseating granulomas with associated calcification and no evidence of doubly refractile bodies.

densities were usually less apparent at the apices and bases of the lung. There was a tendency for concomitant decrease in lymphadenopathy with increase in parenchymal disease.

Approximately one-fourth of the parenchymal disease patterns were fibrotic. This group was most important in terms of prognosis.[18] Certain patients showing this pattern had extensive bilateral parenchymal disease and were particularly susceptible to severe complications. These complications included respiratory failure, cor pulmonale, pneumothorax, and mycetoma formation. Once this fibrotic pattern had developed, it either persisted or worsened. Without previous tissue diagnosis this pattern would have been indistinguishable on the roentgenogram from scarring by tuberculosis, fungal disease, or pneumoconiosis.

Pathologically, the chronic acinar pattern often correlates with extension of the granulomatous process into alveolar spaces.[25] However, almost all disease processes which demonstrate a roentgenographic acinar pattern also show pathologic involvement of the interstitium.[12] This is particularly true of sarcoidosis. Some patterns which appeared on roentgenograms as "acinar" may have been due to superimposition of numerous reticular and nodular densities. This was suggested by the frequent association of reticulonodular and chronic acinar patterns. This possibility should especially be considered when air bronchograms cannot be identified. Approximately one-third of the patients with chronic acinar infiltrates eventually showed clearing. The other two-thirds either showed persistence of acinar infiltrates for the duration of follow-up or progression to fibrosis. The incidence and prognosis of this par-

ticular group has, to our knowledge, not been previously defined.

The large nodular pattern of sarcoidosis is unusual.[6] Despite extensive nodular disease, these patients were relatively asymptomatic. The differential diagnosis included metastatic disease, lymphoma, and septic pulmonary emboli. In 2 cases nodules abutted but did not cross fissures (Fig. 5, *A–C*).

Heart disease in sarcoidosis may be due to direct myocardial involvement, usually manifest by arrhythmias, or it may be secondary to lung disease.[17] In this series, all 7 instances of cardiomegaly were associated with fibrotic pulmonary parenchymal involvement, usually substantiated with clinical and electrocardiographic evidence of cor pulmonale.

The frequency of pleural effusion in sarcoidosis has been reported to be from 1.5 to 2.7 per cent.[5,10,17] In this series, there was a 3.3 per cent incidence of pleural effusion due to sarcoidosis. When a patient with sarcoidosis develops a pleural effusion, the possibility of tuberculosis pneumonia, or congestive heart failure should be considered. However, pleural involvement by sarcoidosis without complicating disease may cause pleural effusion. Analyses of pleural fluid, made in 3 of our 5 cases, were similar to others reported in the literature.[3,15]

SUMMARY

A retrospective roentgenographic analysis was made of 162 patients with a tissue diagnosis of sarcoidosis.

1. Abnormal chest roentgenograms were noted in over 90 per cent of the patients at the time of positive tissue diagnosis.

2. Pulmonary sarcoidosis was most frequently diagnosed in patients 20 through 39 years of age, and was especially common in Negro women.

3. More than 80 per cent of the 150 patients with pulmonary sarcoidosis had lymph node enlargement. Bilaterality was the hallmark of this lymphadenopathy. Bilateral hilar with bilateral paratracheal lymphadenopathy was more common than bilateral hilar with only right paratracheal lymphadenopathy.

4. More than 60 per cent of the 150 patients developed pulmonary parenchymal changes during the course of the disease. A reticulonodular pattern was most common. Fibrotic and chronic acinar patterns were less frequent but common patterns.

5. Pleural effusion due to sarcoidosis was seen in 5 instances.

6. Cardiomegaly, calcified nodes, pneumothorax, lobar atelectasis, and mycetoma were unusual manifestations of pulmonary sarcoidosis.

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EOSINOPHILIC LUNG DISEASE*

(OR HOW TO SLICE P.I.E.)

By LAURENCE A. CITRO, M.D., MICHAEL E. GORDON, M.D., *and* WALLACE T. MILLER, M.D.
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PULMONARY parenchymal disease associated with either blood or tissue eosinophilia has in the past been given a multitude of names. In our efforts to understand this group of diseases, we have been hampered by our terminology.

It is the authors' intention in this paper to present a classification which correlates the roentgenographic and clinical signs of eosinophilic lung diseases (Table 1).

The clinical classification was first presented by Crofton *et al.*[5] in 1952. To this date, however, it has not been generally appreciated by the radiologist that the classification can also be used in conjunction with the roentgenographic findings to arrive at a specific diagnosis rather than terming the disease process the "P.I.E. syndrome."

The problem in the past has been that many authors included in "Löffler's syndrome" diseases which did not fit the original criteria set down by Löffler.[20] The confusion was compounded by applying to these diseases terms such as "eosinophilic pneumonia," "eosinophilic lung disease," and the "P.I.E. (pulmonary infiltrates with eosinophilia) syndrome."[22] The classification of Crofton *et al.*,[5] while not claiming to separate the diseases on the basis of

TABLE I

CLASSIFICATION CORRELATING CLINICAL AND ROENTGENOGRAPHIC FINDINGS

Classification	Clinical Data	Roentgenographic Findings	Etiology
1. *Simple pulmonary eosinophilia* (Löffler's syndrome)	Minimal symptoms, recovery in 1 month; peripheral eosinophilia	Migratory peripheral infiltrates; rapid clearing without treatment	Parasites, drugs, unknown
2. *Prolonged pulmonary eosinophilia* A. Of unknown etiology	Severe symptoms, may be fatal; usually lasts 2 to 6 months, may be recurrent, responds to steroids	Peripheral infiltrates; may progress to diffuse consolidation	Unknown
B. Of known etiology	Variable	Variable	Parasites, fungi, viruses, bacteria, sarcoidosis, exogenous antigens
3. *Tropical eosinophilia*	May have a prolonged course; marked eosinophilia; response to diethylcarbamazine	Disseminated, fine nodules, ranging from 2 to 4 mm.; increased interstitial markings	Microfilaria
4. *Pulmonary eosinophilia with asthma*	Most commonly allergic aspergillosis; infiltrates occurring in the course of chronic asthma or adult onset asthma may be prolonged	Grape-like clusters, recurrent pneumonia, atelectasis	Allergic aspergillosis
5. A. *Polyarteritis nodosa and variants* (hypersensitivity angiitis, classical polyarteritis nodosa, allergic granulomatosis)	Severe symptoms, pulmonary involvement usually occurring before multisystem disease, usually fatal	A. Variation from interstitial markings to peripheral infiltrates to total consolidation	Unknown
B. *Wegener's granulomatosis*		B. Large nodules, cavitation, nodal involvement occasionally	Unknown

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
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TABLE II

MATERIAL

No., Patient	Clinical Data	Roentgenographic Findings	Pathologic Findings
		GROUP 1	
		Simple Pulmonary Eosinophilia	
1. G.M. 30 M	Two weeks of rash, fever, and cough; WBC 15,000 with 25% eosinophilia	Peripheral migratory infiltrates cleared spontaneously	None
2. R.T. 54 F	Asymptomatic patient; WBC 25,000 with 40% eosinophilia	Peripheral infiltrates cleared spontaneously	None
		GROUP 2	
		Prolonged Pulmonary Eosinophilia	
3. D.E. 32 M	A 12 week history of fever, weight loss, and cough; WBC 17,000 with 25% eosinophilia; decreased vital capacity	Bilateral peripheral migratory infiltrates	Lung biopsy: interstitial pneumonitis with round cells and eosinophils
4. E.B. 28 F	Severe symptoms including hypoxemia and required steroids; WBC 10,500 with 14% eosinophilia	Patchy infiltrates; progressed to total lobar consolidation	None
5. J.C. 24 F	Cough, fever; respiratory insufficiency; no response to steroids; WBC 28,000 with 30% eosinophilia	Peripheral infiltrate progressed to diffuse consolidation	Autopsy: organizing pneumonia with eosinophils in the alveoli and interstitium
6. C.O. 57 F	Two months cough, fever, and hypoxia; improvement on steroids; WBC 12,000 with 9% eosinophilia	Diffuse interstitial and alveolar infiltrates, involved mostly upper lobes	Lung biopsy: interstitial pneumonitis, eosinophilic pneumonia
		GROUP 3	
		Tropical Eosinophilia	
7. R.V. 26 M	An Indian student with dry cough; responded to diethylcarbamazine; 16,200 WBC with 50% eosinophilia	Fine nodules measuring 2 to 4 mm. throughout the lungs	None
8. K.Z. 42 M	Wheezing and cough for 1 week; treated with diethylcarbamazine; WBC 6,000 with 42% eosinophilia; decreased vital capacity	Fine nodules throughout both lungs	None
		GROUP 4	
		Pulmonary Eosinophilia with Asthma	
9. N.K. 15 F	Episodic wheezing with cough and fever; WBC 12,000 with 40% eosinophilia	RUL, RLL, and RML consolidation	Aspergilli demonstrated in bronchial plugs
10. S.G. 15 F	Asymptomatic; WBC 12,000 with eosinophilia	Nodular densities in the right upper lobe	Lobectomy; aspergilli found in bronchial plugs
11. C.W. 23 F	Wheezing and cough; WBC 10,000 with 33% eosinophilia	Diffuse grape-like clusters of consolidation	Aspergilli demonstrated in bronchial plugs
		GROUP 5A	
		Polyarteritis Nodosa with Lung Involvement	
12. C.H. 50 M	Cough followed by fever, rash, peripheral neuritis, and hemoptysis; WBC 13,600 with 5% eosinophilia	Central alveolar consolidation initially a lingular infiltrate	Autopsy: necrotizing vasculitis with hemorrhage in the alveoli
13. T.A. 38 F	Three admissions over a 3 year period for cough and fever; peripheral neuritis; WBC from 10,000 to 31,000 with 20 to 80% eosinophilia	RUL infiltrate, LUL infiltrate with perihilar infiltrates; cleared on steroid therapy	Skin biopsy showed a vasculitis
		GROUP 5B	
		Wegener's Granulomatosis	
14. W.L. 48 M	Fever, cough, pharyngitis, otitis and renal failure; WBC 10,000 to 15,000 with 13% eosinophilia	Left perihilar mass; large peripheral nodule	Autopsy: vasculitis and granulomas in the lungs and hilar lymph nodes
15. A.C. 45 F	Arthritis, otitis, fever and renal failure; WBC 8,000 to 13,000 with 16% eosinophilia	Bilateral apical infiltration and cavitation; nodule in the right lung field	Autopsy: noncaseating granulomas in the apices and lungs

WBC = white blood cells; RUL = right upper lobe; RLL = right lower lobe; RML = right middle lobe; LUL = left upper lobe.

etiology, does classify them into 5 clinical groups. The groups are: 1. simple pulmonary eosinophilia; 2. prolonged pulmonary eosinophilia; 3. tropical eosinophilia; 4. pulmonary eosinophilia with asthma; and 5. polyarteritis nodosa.

Using a modification of this classification, the radiologist can correlate the roentgenographic and clinical findings and frequently arrive at a specific diagnosis.

MATERIAL

This review is based upon 15 cases of eosinophilic lung disease seen at the Hospital of the University of Pennsylvania over the past 15 years. There were 9 females and 6 males, ranging in age from 15 to 66 years (Table II).

DISCUSSION

1. SIMPLE PULMONARY EOSINOPHILIA

The diagnosis of simple pulmonary eosinophilia should be limited to those cases which have eosinophilia, roentgenographic changes, minimal symptoms, and rapid spontaneous resolution. The roentgenographic changes have been described as migratory, peripheral,[16] homogeneous densities, which are usually of a combined alveolar and interstitial pattern. They may be unilateral or bilateral and quite often have a pleural based location.[16]

The etiology of this syndrome is thought to be allergic. Cases have been reported in association with parasites including *Ascaris* and *Strongyloides stercoralis*, and various drugs such as para-aminosalicylic acid[6] and nitrofuradantoin.[14]

The pathologic changes have been described as areas of pneumonic consolidation which consist of alveolar exudate containing many eosinophils, mononuclear cells, occasional foreign body giant cells, and *no* associated vasculitis. Eosinophils and other round cells are also found in the interstitium.[2]

A diagnosis of simple pulmonary eosinophilia is warranted in a patient with chest roentgenograms showing rapidly clearing alveolar and interstitial changes, the presence of peripheral eosinophilia and mild symptomatology (Cases 1 and 2; Fig. 1 and 2).

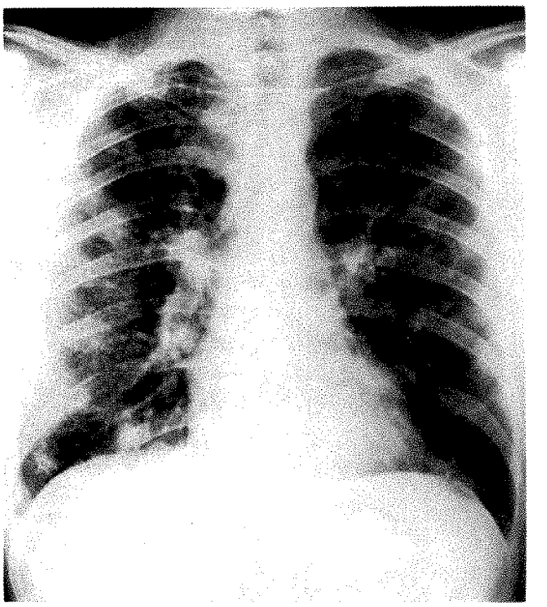


FIG. 1. Case 1. *Simple pulmonary eosinophilia.* A 30 year old male with symptoms of fever, malaise and cough. Bilateral, peripheral migratory infiltrates cleared in 8 weeks. The short course with these roentgenographic changes suggests simple pulmonary eosinophilia.

2. PROLONGED PULMONARY EOSINOPHILIA

Two groups of patients may exhibit prolonged pulmonary eosinophilia—those associated with known etiologic factors, and those with a characteristic clinical and roentgenographic pattern of unknown etiology (chronic eosinophilic pneumonia).

Many diseases can occasionally cause prolonged pulmonary eosinophilia with lung infiltrates. These include drug allergy, parasitic infestation, fungal and bacterial infection,[10] and diseases such as farmer's lung,[17] sarcoidosis, psittacosis, primary atypical pneumonia, mushroom workers' lung, eosinophilic leukemia, and pigeon breeders' disease.[12] These diseases present only with sporadic cases of eosinophilia, and can usually be identified by clinical and laboratory means. While they must be considered in the differential diagnosis of

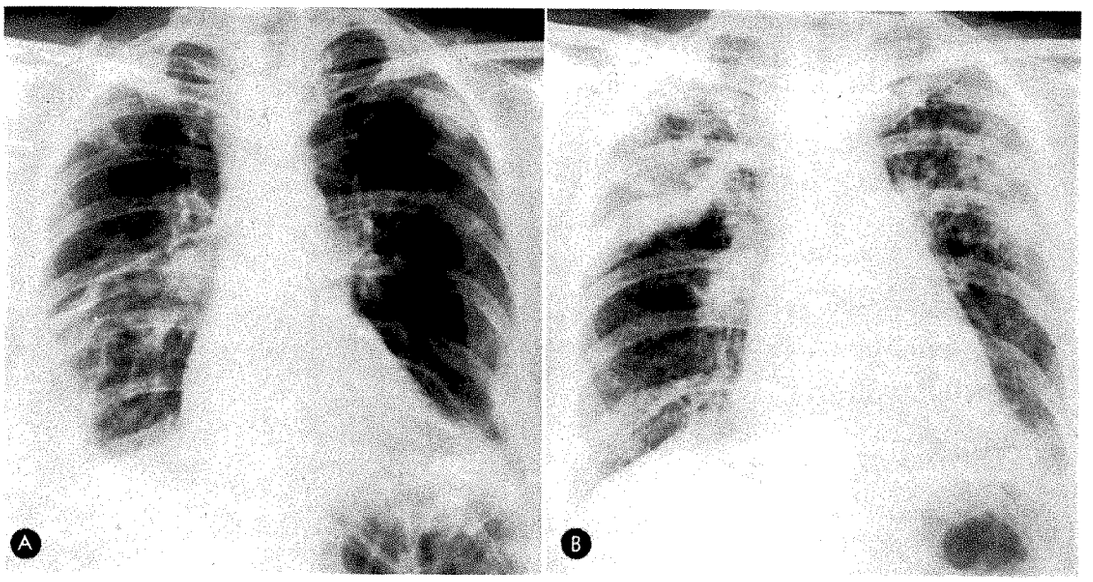


FIG. 2. Case 2. *Simple pulmonary eosinophilia.* (*A* and *B*) A 54 year old asymptomatic female with migratory peripheral infiltrates that cleared spontaneously, placing this patient in the category of simple pulmonary eosinophilia.

eosinophilic lung diseases, in this discussion, we are primarily concerned with chronic eosinophilic pneumonia.

In a few patients chronic eosinophilic pneumonia will overlap simple pulmonary eosinophilia. However, patients with chronic eosinophilic pneumonia usually have more severe symptoms; the symptoms and roentgenographic changes persist longer; the outcome may be fatal; and vigorous therapy is required. It is of utmost importance to recognize this syndome since lack of appropriate therapy may be fatal (Case 5; Fig. 4, *A* and *B*).

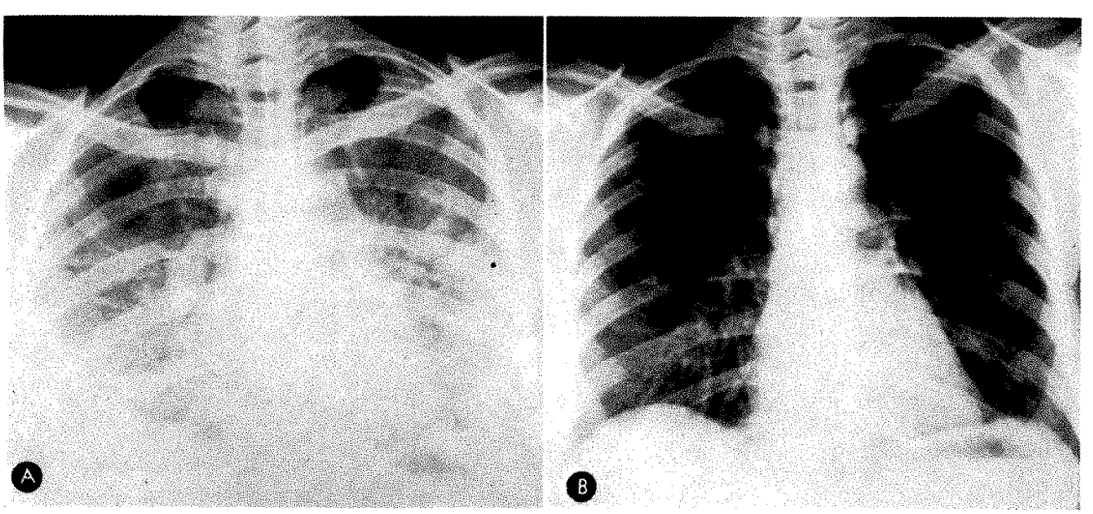


FIG. 3. Case 4. *Prolonged pulmonary eosinophilia.* (*A* and *B*) A 28 year old black female who was quite symptomatic with fever, wheezing and hypoxemia that required oxygen and steroids. The chest roentgenograms show patchy nonsegmental infiltrates which progressed to total lobar consolidation (*A*) that cleared 2 weeks later (*B*) as the patient became asymptomatic. The combination of a symptomatic course requiring oxygen and steroid therapy is indicative of chronic eosinophilic pneumonia.

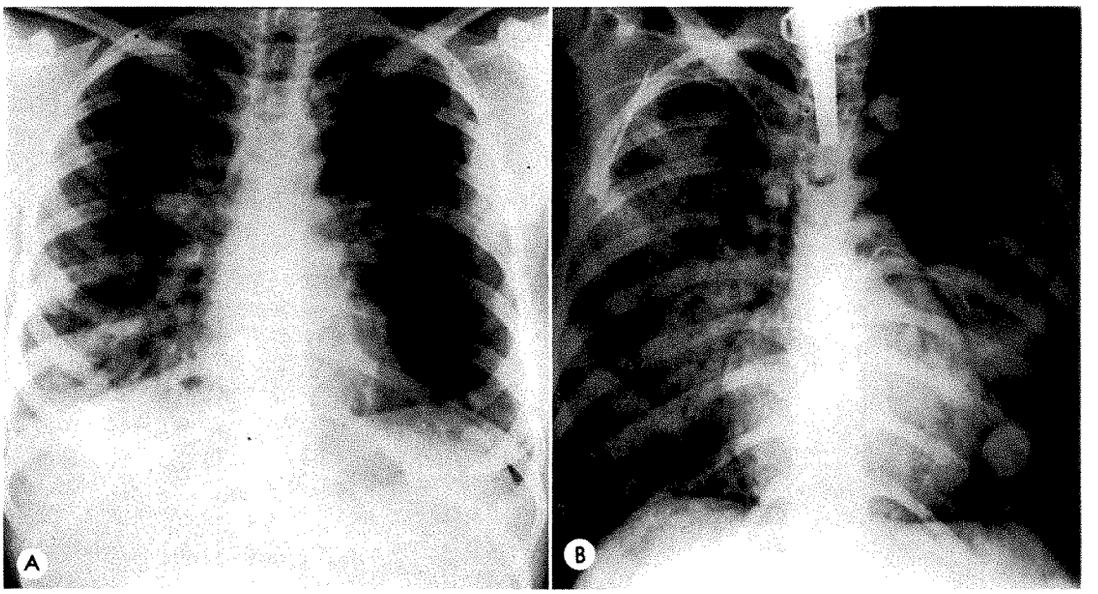


Fig. 4. Case 5. *Prolonged pulmonary eosinophilia.* (*A* and *B*) A 24 year old female with a 6 week history of cough, fever and respiratory insufficiency. Steroids were started only after the patient had a cardiac arrest; the patient expired 2 days later. The peripheral infiltrate (*A*) progressed to total lung consolidation (*B*). The roentgenographic appearance combined with the severe clinical course is indicative of chronic eosinophilic pneumonia, which was confirmed at autopsy.

Nine patients with chronic eosinophilic pneumonia have been described by Carrington *et al.*[4] Their presenting symptoms included high fever, night sweats, weight loss, and dyspnea. Two-thirds of the patients had a peripheral eosinophilia. The disease was considered life threatening in at least 1 patient and fatal cases have been reported.[19] Pulmonary function tests show restrictive lung disease with decreased vital capacity, "alveolar-capillary block" with hypoxemia, and decreased diffusing capacity (Cases 3, 4, 5, and 6).

The pathologic changes consist of eosinophilic exudation into the alveoli and interstitium, associated with vasculitis of small vessels. Organization with fibrous tissue in the alveoli and interstitium is also a feature.[4,19]

The roentgenographic findings have been well described.[4,19] In general, the findings on any single roentgenogram are indistinguishable from simple pulmonary eosinophilia. On serial roentgenograms, distinguishing features include a prolonged course, rapid clearing with steroids, and frequent recurrence in the same area upon steroid withdrawal. Carrington *et al.*[4] have emphasized the peripheral nature of the infiltrates by terming the pattern "the negative of pulmonary edema." In our 4 cases, only 1 presented in this manner. The other cases showed either diffuse lung disease or segmental infiltrates (Cases 4, 5, and 6; Fig. 3, 4, and 5).

The radiologist should suspect chronic eosinophilic pneumonia when encountering a patient with eosinophilia, severe or life threatening symptomatology, and a prolonged course associated with the previously described roentgenographic changes. The progression from peripheral infiltrates to almost complete consolidation is not seen in simple pulmonary eosinophilia.

3. TROPICAL EOSINOPHILIA

Tropical eosinophilia was first described as a symptom complex by Weingarten.[29] Donohugh[8] states that the criteria for diagnosis are: 1. recent residence in the tropics; 2. pulmonary symptoms; 3. an eosinophil count in excess of 2,000/mm.^{3} of

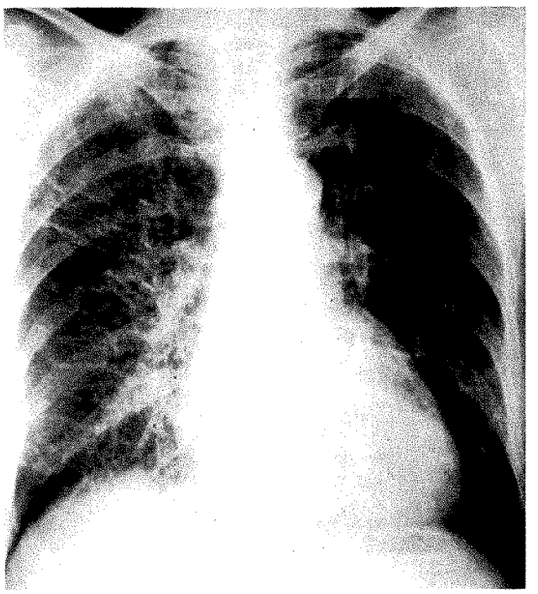


FIG. 5. Case 6. *Prolonged pulmonary eosinophilia.* A 57 year old female with a prolonged course of cough and malaise, who became less symptomatic after steroid treatment. The chest roentgenogram shows a disseminated interstitial and alveolar pattern that cleared after steroids, suggesting that this patient had chronic eosinophilic pneumonia, which was confirmed by a lung biopsy.

blood; 4. a positive filarial complement fixation test; and 5. good clinical response to diethylcarbamazine.

Pulmonary symptoms such as nocturnal cough, asthma, and dyspnea dominate the clinical picture. If untreated, the disease may run a prolonged course, and the end result may be pulmonary fibrosis.

The etiology of the disease, although unproven, is thought to be due to microfilaria.[8] This is supported by the finding of microfilaria in nodular lesions in the lungs,[28] the specific response to antifilarial drugs and the positive complement fixation test.

The pathologic changes seem to be related to the duration of the illness. Patients with a short history of symptoms show a histiocytic interstitial infiltration of the lung parenchyma; patients who have had a longer history show peribronchial and perivascular accumulations of eosinophils—"an eosinophilic bronchopneumonia."

Roentgenographically, the changes are quite distinctive. The vast majority of the cases will show increased interstitial markings and disseminated 2 to 4 mm. nodules throughout both lungs[18] (Cases 7 and 8; Fig. 6). Both the increased interstitial markings and the nodules are more pronounced in the lower lung fields with relative sparing of the apices. Infrequently, there may be patchy areas of consolidation superimposed upon these changes. Few, if any, of the other eosinophilic lung diseases exhibit this roentgenographic pattern. Typically, these changes will resolve in 1 or 2 months after therapy.

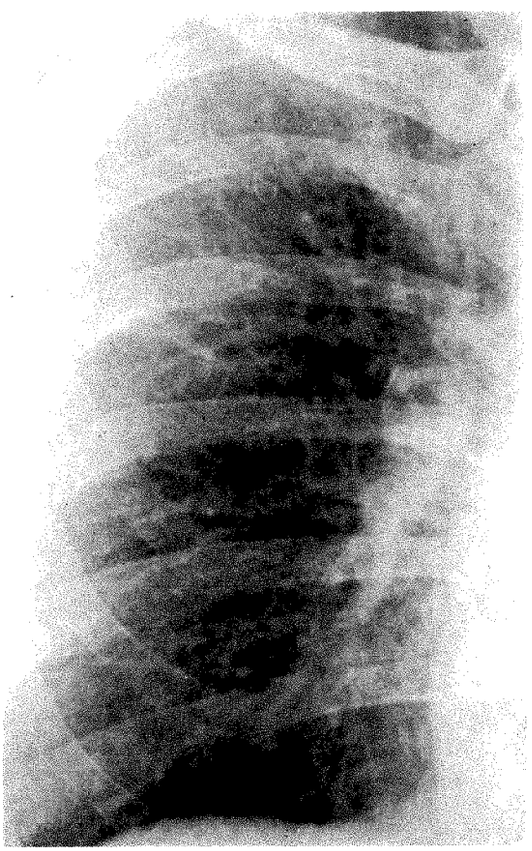


FIG. 6. Case. 8. *Tropical eosinophilia.* Roentgenogram of this 42 year old male who had been to India and had symptoms of wheezing and cough, shows a disseminated fine nodular pattern. The history of travel to India and this nodular pattern is suggestive of tropical eosinophilia. This was confirmed by the disappearance of symptoms and respiratory findings after treatment with diethylcarbamazine.

4. PULMONARY EOSINOPHILIA WITH ASTHMA

Eosinophilia and infiltrations of the lung can occur in asthmatics. Ford[11] described 20 cases of pulmonary eosinophilia in 5,702 asthmatics which he labelled as Löffler's syndrome. Scadding[24] described "intrinsic" and "extrinsic" asthmatics and stated that a high proportion of eosinophilic lung disease in extrinsic asthmatics is due to allergic aspergillosis.

Allergic aspergillosis is by far the most common cause of pulmonary eosinophilia in asthmatics in the authors' opinion. Clinically, the disease may present as adult onset asthma or exacerbation of long standing asthma. The symptoms include increased sputum production, wheezing, fever, cough and eosinophilia. Steroids offer prompt relief. The diagnosis can be made by finding aspergilli in the bronchial plugs.

Roentgenographically, it can present as recurrent pneumonitis and/or atelectasis of one or more segments of the lung (Case 9). Specific findings observed in some patients consist of a nodular pattern resembling a cluster of grapes radiating from the hilum (Cases 10 and 11; Fig. 7).

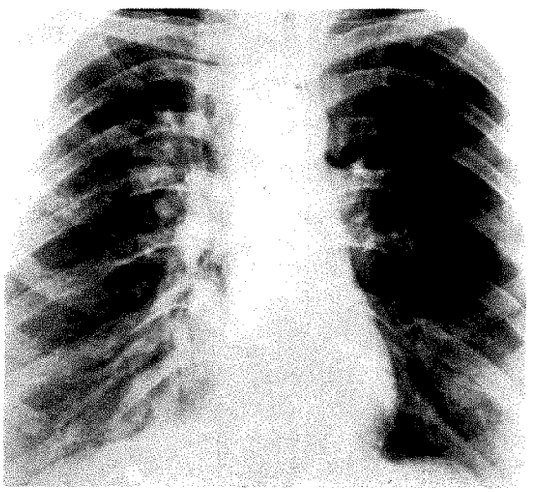


FIG. 7. Case 11. *Allergic aspergillosis.* A 23 year old female with coughing and wheezing has a "grape-like" cluster of consolidation which cleared with steroids. This pattern is quite suggestive of allergic aspergillosis, which was proved by microscopy of a bronchial plug.

A history of pulmonary eosinophilia associated with chronic asthma, or adult onset asthma, correlated with the above roentgenographic findings strongly suggests the diagnosis of allergic aspergillosis.

5. POLYARTERITIS NODOSA (NECROTIZING ANGIITIDES)

There have been reports in the literature of polyarteritis nodosa with lung involvement.[23] Some authors take exception to this and state that classical polyarteritis nodosa rarely, if ever, involves the lung.[1] Zeek[30] has offered a classification which may clear the confusion. She stated that the group of diseases termed "necrotizing angiitides" could be subdivided as follows: 1. hypersensitivity angiitis; 2. allergic granulomatosis and angiitis; 3. rheumatic arteritis; 4. polyarteritis nodosa; and 5. temporal arteritis. The groups are pathologically distinguished by the types of vessels involved and the presence or absence of associated tissue necrosis and granulomas. For the present discussion, we are concerned with hypersensitivity angiitis, classical polyarteritis nodosa, and allergic granulomatosis and angiitis.

Pathologically, classical polyarteritis nodosa rarely involves the pulmonary arteries, but typically involves small and medium muscular systemic arteries.[1] Extravascular lesions (granulomas) and necrotizing alveolitis are not features of classical polyarteritis nodosa. In hypersensitivity angiitis, the arteritis involves the pulmonary arteries and small systemic vessels. Hypersensitivity angiitis may be associated with a necrotizing alveolitis. Allergic granulomatosis and angiitis generally have the same vascular pathology as hypersensitivity angiitis but also exhibit extravascular tissue necrosis and granulomas.

To the authors' knowledge, there has been no roentgenographic pathologic correlation of these entities reported in the literature. From the present point of view, we shall term all of these diseases polyarteritis nodosa with pulmonary involvement, recognizing that we are dealing with

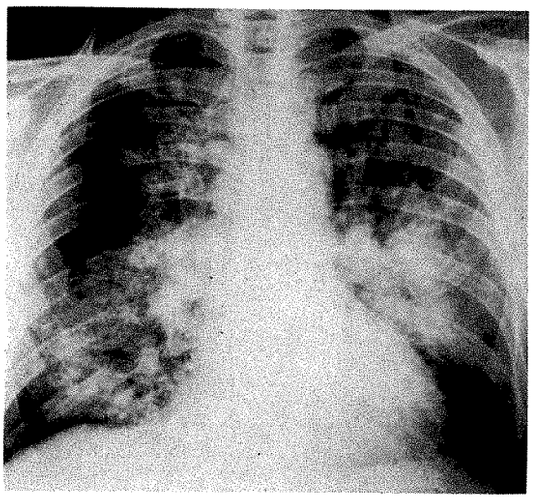


FIG. 8. Case 12. *Polyarteritis nodosa with pulmonary involvement.* Central alveolar consolidation, the "bat wing" appearance, is present in this 50 year old male who expired after progression from a cough and upper respiratory infection to hemoptysis and respiratory insufficiency. This roentgenographic pattern is not specific for polyarteritis nodosa with lung involvement, but is suggested in a patient with eosinophilia, alveolar consolidation, and systemic disease. Autopsy showed changes consistent with hypersensitivity angiitis.

a group of interrelated diseases with varying manifestations and that the cases with pulmonary involvement are probably hypersensitivity angiitis or allergic granulomatosis.

Approximately 20 to 30 per cent of the cases of polyarteritis nodosa have peripheral eosinophilia;[7,23] 25 per cent of the cases have pulmonary involvement at autopsy; and a combination of eosinophilia and pulmonary infiltration will occur in 10 per cent.[7]

Clinically, these patients with polyarteritis nodosa with lung involvement usually present with the pulmonary symptoms before other organ involvement. Eosinophilia may be quite marked and persistent.

The roentgenographic changes in polyarteritis nodosa have been variously described.[9,13] We think that the changes described as increased linear markings with fine nodulation (generally in patients without pulmonary symptoms) are seen in patients with classical polyarteritis nodosa. Nonsegmental, parenchymal consolidations which often clear only to reappear are more characteristic of hypersensitivity angiitis. Generally, the more pronounced roentgenographic changes appear only in those patients with pulmonary symptoms.[23]

Divertie and Olsen[7] compared 30 cases of what they termed Löffler's syndrome, but which included some cases of prolonged pulmonary eosinophilia, to 13 cases of polyarteritis nodosa with lung involvement. They found the following clinical characteristics to be helpful in distinguishing the 2 groups: age—patients with polyarteritis nodosa were 15 years older on an average; hemoglobin—almost all the patients with polyarteritis nodosa with lung involvement were anemic; blood urea nitrogen values—50 per cent of the patients with polyarteritis nodosa were

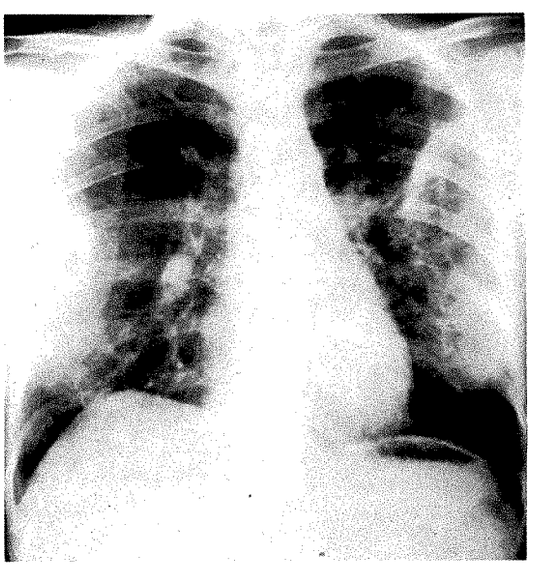


FIG. 9. Case 13. *Polyarteritis nodosa with lung involvement.* A 38 year old female had several admissions for cough and fever. Finally, after steroid therapy, she improved. The chest roentgenogram shows peripheral infiltrates which were migratory. These findings are consistent with polyarteritis nodosa with lung involvement. The clinical diagnosis was substantiated by a muscle and skin biopsy.

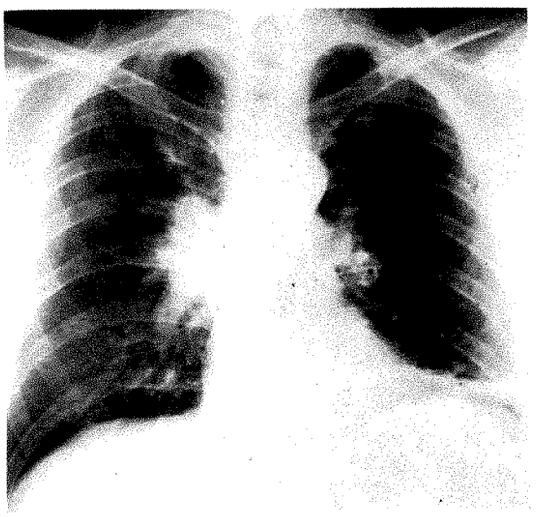


Fig. 10. Case 14. *Wegener's granulomatosis.* This 48 year old male presented with fever, cough, epistaxis, and renal failure and later died. Roentgenogram reveals a right perihilar mass, found to be Wegener's granulomatosis on autopsy.

uremic. Hemoptysis occurred in 60 per cent of the patients with polyarteritis nodosa, but only in 12 per cent of the patients with simple or prolonged pulmonary eosinophilia.

Polyarteritis nodosa with lung involvement can present as eosinophilic lung disease (Cases 12 and 13; Fig. 8 and 9). The roentgenographic appearance is similar to prolonged pulmonary eosinophilia; however, the presence of multisystem involvement is indicative of polyarteritis nodosa with lung involvement and the diagnosis can be suggested on this basis.

Wegener's granulomatosis is not usually included in the differential diagnosis of eosinophilic lung diseases. Most authors agree that eosinophilia is not a prominent feature of this disease;[15] however, Walton[27] found peripheral eosinophilia in 40 per cent of his cases. The authors have seen 2 cases of Wegener's granulomatosis which had peripheral eosinophilia (Cases 14 and 15; Fig. 10 and 11). One case presented with perihilar masses on the chest roentgenogram, and the second had bilateral apical infiltration with cavitation associated with a nodule in the right middle lobe. These findings have previously been described in the literature.[3,21]

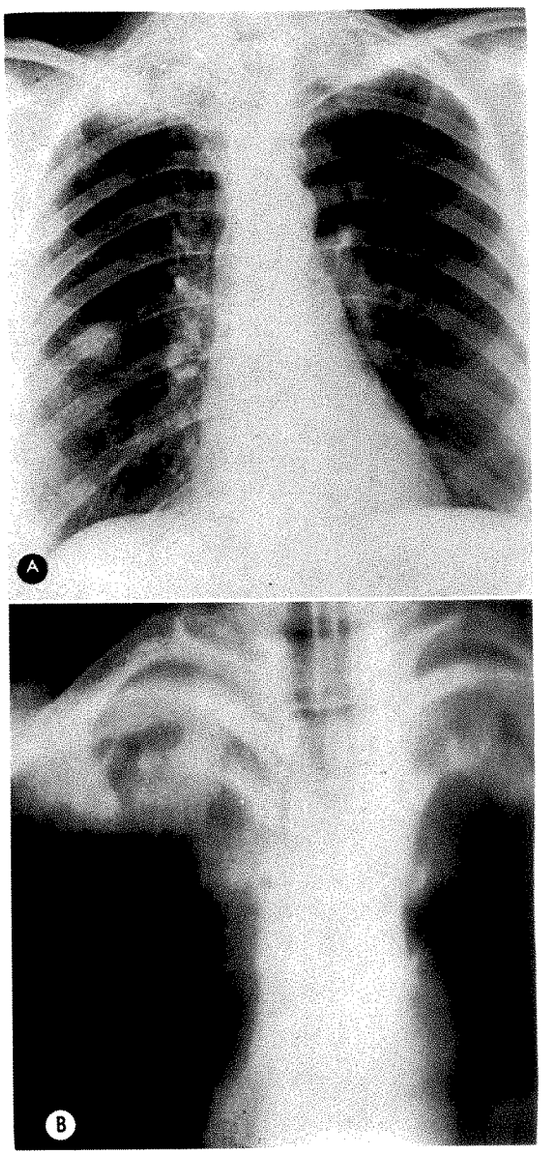


Fig. 11. Case 15. *Wegener's granulomatosis.* (*A* and *B*) A 45 year old female presented with arthritis, otitis, fever, and renal failure. Chest roentgenogram (*A*) reveals a nodule in the right lung, and bilateral apical infiltrations with cavitation (*B*). Skin tests and sputum tests were consistently negative for tuberculosis. The roentgenographic and clinical features are very suggestive of Wegener's granulomatosis which was found at autopsy.

Occasionally, a patient may present with symptoms similar to polyarteritis nodosa; however, if the chest roentgenogram reveals relatively large pulmonary nodules with or without cavitation, the diagnosis of Wegener's granulomatosis is suggested.

SUMMARY

A categorical approach to eosinophilic lung disease is discussed.

Using the clinical and roentgenographic information, the numerous causes of this syndrome can be separated into 5 groups: 1. simple pulmonary eosinophilia; 2. prolonged pulmonary eosinophilia; 3. tropical eosinophilia; 4. asthma associated with pulmonary eosinophilia; and 5. polyarteritis nodosa and its variants.

Fifteen illustrative cases are presented.

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THE ROENTGENOGRAPHIC MANIFESTATIONS OF PULMONARY OPPORTUNISTIC INFECTIONS*

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A RELATIVELY new field of medicine in the form of opportunistic infectious disease has evolved with the advent of transplantation, increasing survival of individuals with neoplastic diseases and an ever increasing array of more potent chemotherapeutic and immune suppressing agents. Since the mid 1960s, a spiraling incidence of these opportunistic infections has been reported in the medical literature;[26] however, little can be found in the radiologic literature emphasizing the dilemma in attempting to distinguish between the effects of a primary disease, the complications of therapy, or opportunistic infection.[24]

It is the purpose of this paper to review 52 instances of well documented opportunistic lung disease and analyze the roentgenologic features involved in their presentation and evolution.

In the context of this article, opportunistic disease is defined as an infection in a host with altered defense mechanisms, tempered either by his primary disease or subsequent therapy. The offending organisms found in such circumstances may thus be saprophytes or pathogens which become more virulent under the conditions of altered host resistance. Differential diagnostic considerations must be placed in their appropriate setting to distinguish between the complications of the underlying disease, its therapy and the different mode of presentation of these opportunistic organisms than when they are seen as primary pathogens.

In recent years the increased frequency of opportunistic infection has been well documented in many articles.[18,26,29,31,36,37,53] Of particular concern is our inability to diagnose this disease process ante mortem, as well as the frequency by which opportunistic lung disease is found to be the primary cause of death with the underlying disease apparently under control.[35,36]

MATERIAL AND METHOD

The cases were collected at random from a far larger group in our review of patients with diseases associated with altered immune mechanisms, postmortem records, bacteriologic files, and transplantation summaries. The broad categories of underlying diseases involved in this review are summarized in Table I.

Fifty-two examples of opportunistic pulmonary inflammatory disease were included in this study based on good documentation of the underlying organism, adequate clinical information as well as satisfactory roentgenographic studies encompassing the problem. Table II gives the organisms responsible, listing 52 separate episodes in 49 patients, with 3 individuals having temporally separate episodes of opportunistic pulmonary disease. Our random process of case selection, therefore, does not include all opportunistic infections at the University of Utah Medical Center, nor reflect the incidence for each underlying disease.

Table III outlines the method by which the diagnosis of these organisms was established. Each case was analyzed as to the status of the underlying disease, its therapy, the onset of pulmonary presenting signs and symptoms of the opportunistic disease, method of diagnosis and the response to treatment. Roentgenographic

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TABLE I

BROAD CATEGORIES OF UNDERLYING DISEASES

Underlying Diseases	Patients
Leukemia	11
Lymphoma	4
Renal transplant	17
Other malignancies	4
Miscellaneous	13
Total	49

TABLE II

OFFENDING ORGANISMS

Pneumocystis carinii	12
Nocardia	7
Phycomycetes	3
Cytomegalic inclusion disease	5
Aspergillus	4
Bacterial	18
Coccidioides immitis	1
Candida	2
Total	52

studies on each case were analyzed as to the presenting appearance, progression and resolution of each opportunistic episode. The 16 cases discovered by sputum analysis were all confirmed by either response to therapy, course of the disease or postmortem examination. Each of the 15 cases confirmed at autopsy (29 per cent) had roentgenographic studies ante mortem considered adequate for retrospective review. In all instances, the opportunistic pulmonary disease was felt to be responsible for the major roentgenographic and pathologic changes.

CLINICAL AND BACTERIOLOGIC CONSIDERATIONS

A brief review of each of the less common organisms concerned in this study is essential to the understanding by the radiologist of the presentation and course of these opportunistic infections.

I. PNEUMOCYSTOSIS

Pneumocystis carinii is the only protozoan member of the class Haplosporea pathogenic for man.[17] Practically nothing is known about the epidemiology and transmission of this parasite in humans.[42,43] Experimental work with rats has shown that prolonged treatment with corticosteroids can activate latent infections of *Pneumocystis carinii*.[20] It is interesting to speculate that this mechanism of immune suppression may be the experimental counterpart of the disease in humans.

Pneumocystosis occurs in 2 clinical settings in humans. An epidemic form in Europe has been described in premature or debilitated infants, presenting as plasma cell pneumonia.[17,42] Many of the earlier roentgenologic descriptions of pneumocystosis arose from studies of this primary form

TABLE III

METHOD OF DIAGNOSIS*

	Biopsy Needle Positive	Open Lung Biopsy	Sputum Examination	Autopsy	Other
Nocardia (7)	4/5	1/1	1		1
Pneumocystis (12)	3/3	5/5	1	3	
Aspergillus (4)		1/1		3	
Bacterial (18)	2/2		13	3	
C.I.D. (5)	0/2	1/1		3	
Phycomycetes (3)		*2/2		1	
Coccidioides immitis (1)	0/1		1 tracheal		
Candida (2)				2	
Totals	9/13	10/10	16	15	1

* Two explorations to document.

of the disease, describing it as largely interstitial in presentation. This experience has been translated to the opportunistic form of the disease and we feel it to be in error. The other human form of *Pneumocystis carinii* infection in man occurs as an opportunistic process seen in patients with primary or acquired alterations in host defenses.[30,31,37,42,43,45] It may be that intensive immunosuppressive therapy activates inapparent infestations of *Pneumocystis carinii*, giving rise to clinically significant disease.[37]

The clinical presentation is quite typical. The patient develops dyspnea, tachypnea, a low-grade fever and a dry cough. Cyanosis is usually associated; however, few auscultatory findings are noted aside from occasional dry rales.[16,42,43,47] Blood gas analysis discloses an alveolar-capillary block-like syndrome.[42,43] The organisms are rarely recovered from the sputum alone, and diagnosis usually demands transtracheal aspiration, lung aspiration, lung biopsy or endobronchial brush biopsy.[7,15,30,40]

The pathology seen in cases of *Pneumocystis carinii* pulmonary disease is principally confined to the alveolar areas.[16] The organisms are stained best with Gomori's methanamine silver stain and are found predominantly within the alveoli. The alveolar spaces are filled with a pink, foamy material with little in the way of an interstitial inflammatory response.

II. NOCARDIOSIS

Pulmonary nocardiosis is most frequently caused by *Nocardia asteroides* which is an aerobic, gram positive, partially acid-fast branching Actinomycetes.[14] These organisms are common in nature and have been isolated widely from soil specimens in North America.[11] In marked contrast to phycomycosis and aspergillosis, Nocardia species are rarely found as contaminants in the respiratory tract.[39]

The primary site of infection in man is usually the lung with about one-third of these infections remaining confined to the respiratory system.[36] The other common site of metastatic spread occurs to the central nervous system.[48]

The pathologic response in the involved tissue is one of extensive suppuration and abscess formation.[14] Although nocardiosis can be present as a primary disease, recent reports have emphasized its role as an opportunist.[52]

III. PHYCOMYCOSIS

The class Phycomycetes contain fungi with non-septate hyphae.[38] Three genera within this class, which are often the cause of the clinical disease phycomycosis, are Rhizopus, Mucor and Absidia. These 3 genera are omnipresent in man's surroundings, but only rarely are they associated with disease.[1,38] Most cases of phycomycosis are discovered in people with diabetic ketoacidosis, and the majority of these individuals present with a rhinocerebral form of the disease.[1,5,36,38,45] Patients with leukemia or lymphoma as well as those being treated with immune suppressive therapy more often develop the pulmonary form of phycomycosis.[1,34,36] The reasons for this occurrence are not known.

In either cranial or pulmonary locations, the pathology is similar. These organisms tend to invade blood vessels and lymphatics leading to the formation of septic thrombi, infarction and tissue necrosis.[4,38,44] Due to the ubiquitous nature of these organisms, diagnosis depends upon the demonstration of invasive fungi with characteristic morphology in biopsy specimens and fungal growth from lung tissue, transtracheal or lung aspirates.[51]

IV. CYTOMEGALIC INCLUSION DISEASE (C.I.D.)

The cytomegaloviruses belong to the herpes group of viruses and are morphologically indistinguishable from herpes simplex and varicella viruses.[50] Cytomegalovirus infections are present in approximately 1 per cent of newborn infants in this country, increasing to 10 to 20 per cent of children by the time they reach the third or fourth month of life.[49] Most

of these infections are clinically asymptomatic. The propensity of the cytomegalovirus to produce latent infections and their subsequent activation in a compromised host may explain some of the disease now being reported as opportunistic infections.[41] Similarly, the virus may enter the host *via* blood transfusions or organ transplantation.[3,41]

Infection in the compromised host occurs in 2 clinical forms, one being a heterophile negative mononucleosis-like syndrome[6] and the other a pulmonary infection. The symptomatology of the pulmonary form of the disease is nonspecific and only rarely will pure cytomegalovirus lung infection be considered as the primary cause of death.[27]

Pathologically, the pneumonic form of the disease is characterized by mononuclear cell proliferation with cytomegaly. Severe infections are accompanied by local hemorrhage and necrosis.[36] At present, there is no specific therapy for this disease process.

V. ASPERGILLOSIS

The class of Fungi Imperfecti contains organisms with septate hyphae.[2] The species of Aspergillus which cause human disease reside in this class and the presence of septate hyphae allows microscopic differentiation from Phycomycetes. The most common species involved in human disease is *Aspergillus fumigatus*.

Since the Aspergillus species are ubiquitous in man's environment and are frequently encountered as contaminants of respiratory secretions,[13] the diagnosis rests upon the isolation of these organisms from body fluids or the demonstration of the fungus as an invader in tissue sections.[26] The lung is the most common site for infection. The clinical-pathologic spectrum of pulmonary aspergillosis runs the gamut from a relatively asymptomatic solitary granuloma to a severe necrotizing bronchopneumonia.[51] Aspergillosis as an opportunistic process appears to behave differently than the previously described primary forms of the disease.[19,21,52] In the opportunistic setting, aspergillosis tends to take on a more aggressive clinical and roentgenologic course. It appears to be more common as an opportunistic problem in association with neoplasms, as were 3 of our 4 cases.[26]

ROENTGENOGRAPHIC FINDINGS

Of primary interest were the roentgenographic studies concerning the group of *Pneumocystis carinii*, *Nocardia*, *Phycomycetes*, cytomegalic inclusion disease, *Aspergillus*, and the bacterial organisms.

I. PNEUMOCYSTOSIS

In only 4 of the 12 cases were we able to distinguish retrospectively the interstitial, perihilar origin of this process described so frequently in the literature.[8,10,18,23,28,33,46] In virtually every case the dominant roentgenographic pattern from its beginning was one of an alveolar process. This initial phase often was one of an ill-defined "acinar" pattern resembling interstitial disease but rapidly progressed to confluence. As has been reported earlier, the consolidative phase may involve the entire lung but until late, usually spares the extreme peripheral portions of the lung parenchyma (Fig. 1, *A–C*). Except for 1 case, no pleural effusions were noted although most of these sequential studies were anteroposterior roentgenograms made with the portable unit only. There was no evidence for mediastinal lymphadenopathy. In 1 case, the disease remained confined to the right lower lobe as a nonspecific pneumonic infiltrate. At postmortem examination this was proved to be a *Pneumocystis carinii* infection.

Emphasis should thus be placed on the alveolar presenting features and subsequent evolution of *Pneumocystis carinii* pulmonary involvement which conforms to its pathologic presentation.[9,18,32] With the realization that this process is alveolar in form, and fortified by the constancy of the presenting clinical features, radiol-

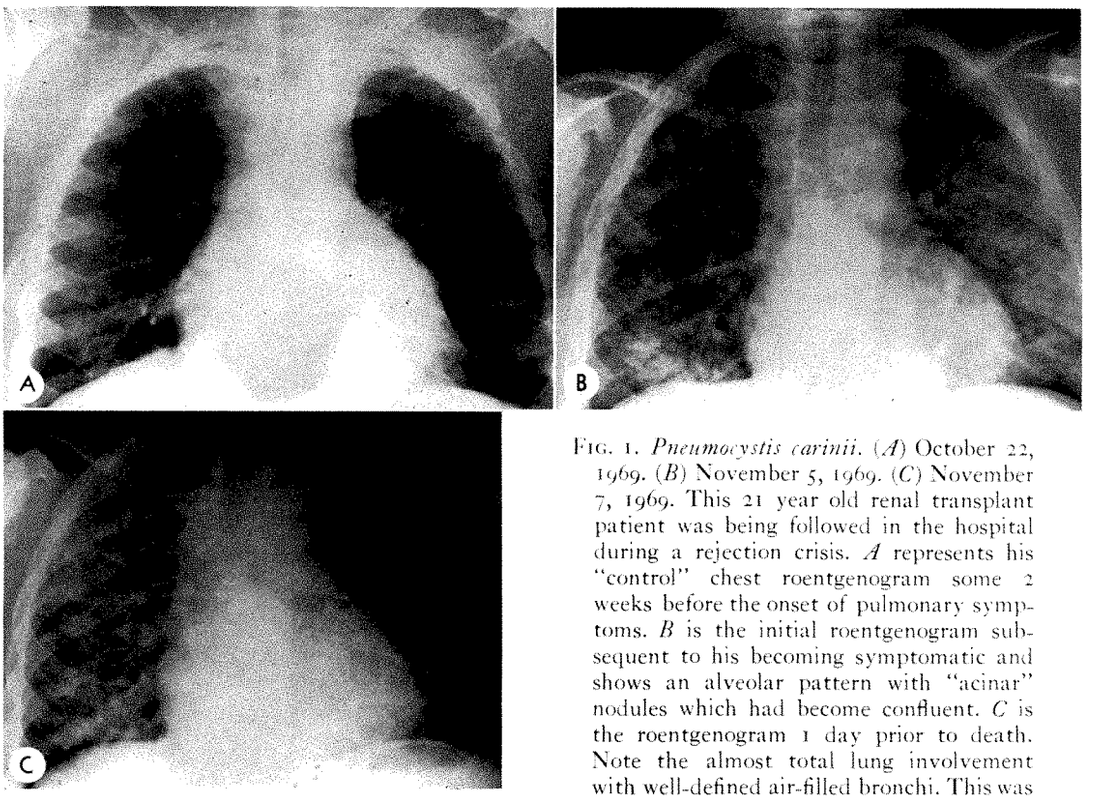


Fig. 1. *Pneumocystis carinii*. (*A*) October 22, 1969. (*B*) November 5, 1969. (*C*) November 7, 1969. This 21 year old renal transplant patient was being followed in the hospital during a rejection crisis. *A* represents his "control" chest roentgenogram some 2 weeks before the onset of pulmonary symptoms. *B* is the initial roentgenogram subsequent to his becoming symptomatic and shows an alveolar pattern with "acinar" nodules which had become confluent. *C* is the roentgenogram 1 day prior to death. Note the almost total lung involvement with well-defined air-filled bronchi. This was quite typical of the roentgenographic features of our 12 *Pneumocystis* patients.

ogists should then be able to significantly narrow their differential considerations. The main roentgenographic differential problems include diffuse alveolar hemorrhage and the effects of pulmonary edema or uremic lung disease. Diffuse alveolar hemorrhage may exactly mimic the above described changes of *Pneumocystis carinii* pneumonia; however, the clinical setting should be vastly different (Fig. 2).

II. NOCARDIOSIS

The 7 cases of nocardiosis resembled those reported by Grossman *et al.*[25] There were 2 examples of an alveolar infiltrative process, lobar in distribution. Four examples of cavitary lesions were noted, 1 of which involved a mass, with the remaining 3 occurring in lobar infiltrative areas (Fig. 3). One case demonstrated an empyema, together with mediastinal lymphadenopathy and a superior vena caval obstruction. This case was confused clinically with a primary lung tumor. This latter example may indeed represent an instance of primary nocardiosis; however,

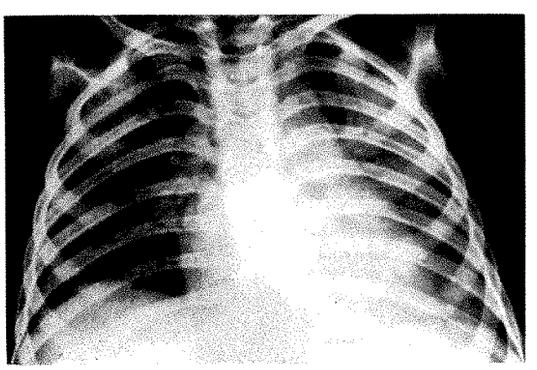


Fig. 2. *Pneumocystis pneumonia*. The differential considerations in a case of diffuse alveolar disease are: 1. pneumocystis pneumonia; 2. uremic lung disease; 3. intraalveolar hemorrhage; 4. congestive heart failure. The clinical setting should provide the main clues in roentgenographic differentiation. Also, the lack of a pleural effusion with *Pneumocystis* and its frequent presence in entities 2, 3 and 4 are helpful differential points.

it was superimposed on chronic obstructive lung disease. Of the group of 7 cases, all were diagnosed ante mortem, with only 1 appearing to represent a treatment failure, subsequently confirmed at postmortem examination.

The roentgenologic differential considerations in our group of nocardiosis cases would include aspergillosis, phycomycosis, necrotizing bacterial pneumonias (to be described subsequently), as well as excavation within a primary or metastatic tumor. As 5 of the 7 examples of nocardiosis were discovered in patients having undergone renal transplantation, a cavitary focus in an infiltrative or nodular pulmonary lesion should strongly suggest the diagnosis of nocardiosis, particularly in a transplant recipient (Fig. 4).

III. PHYCOMYCOSIS

Three cases from the Class Phycomycetes were reviewed (Table II). In 1 individual, a juvenile onset diabetic, mucormycosis was documented. A second individual with mildly elevated blood sugar values was shown to have an undifferentiated type of Phycomycetes at postmortem examination. This patient had been treated for an ill-defined left upper lobe infiltrate presumed to be of tuberculous origin. The third individual with chronic glomerulonephritis on steroids was found to have an Absidia organism causing his pulmonary disease. Both the Mucor and Absidia infections evolved rapidly into cavitary lesions. In the example of mucormycosis, a sizeable central mass developed within a large cavity. Rapid enlargement of both the mass and cavity occurred in spite of open surgical debridement. Terminally the lesion eroded into the right main stem bronchus and perforated the superior branch of the right pulmonary artery (Fig. 5, *A–C*). The Absidia organism produced bilateral pulmonary disease with both empyemas and multiple cavitary lung abscesses. No response to medical and surgical therapy was visible on serial chest roentgenograms, and

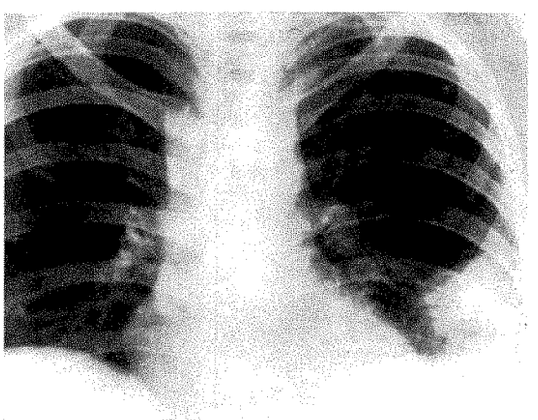


FIG. 3. *Nocardiosis*. This 24 year old renal transplant patient presented with fever and left pleuritic chest pain. Her roentgenogram on admission shows an infiltrative process with an eccentric cavitary focus. *Nocardia asteroides* was found on percutaneous biopsy 5 days later. The lesion gradually faded after months of triple sulfa therapy. Both the roentgenographic appearance of a cavitary infiltrative process and the slow resolution were typical of our group of 7 cases of nocardiosis.

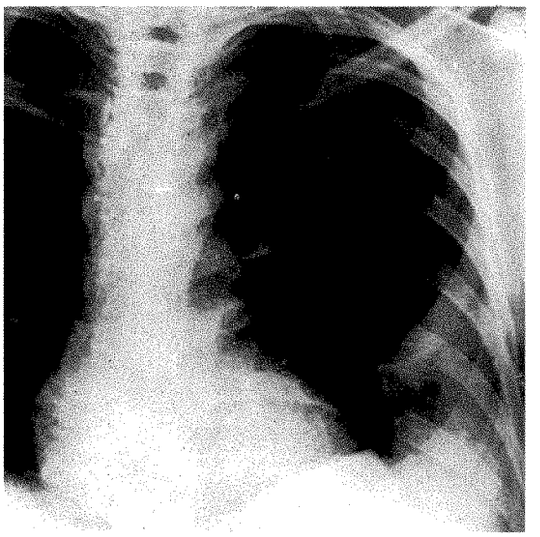


FIG. 4. *Nocardiosis*. The differential considerations in the cavitary infiltrative process are: 1. nocardiosis (lobar infiltrate or cavitary mass); 2. aspergillosis; 3. phycomycosis; 4. necrotizing bacterial pneumonia; 5. excavating primary or metastatic tumor. Aspergillosis usually presents with nodular lesions which excavate. The course both clinically and roentgenographically should allow one to exclude phycomycosis and the necrotizing bacterial pneumonias.

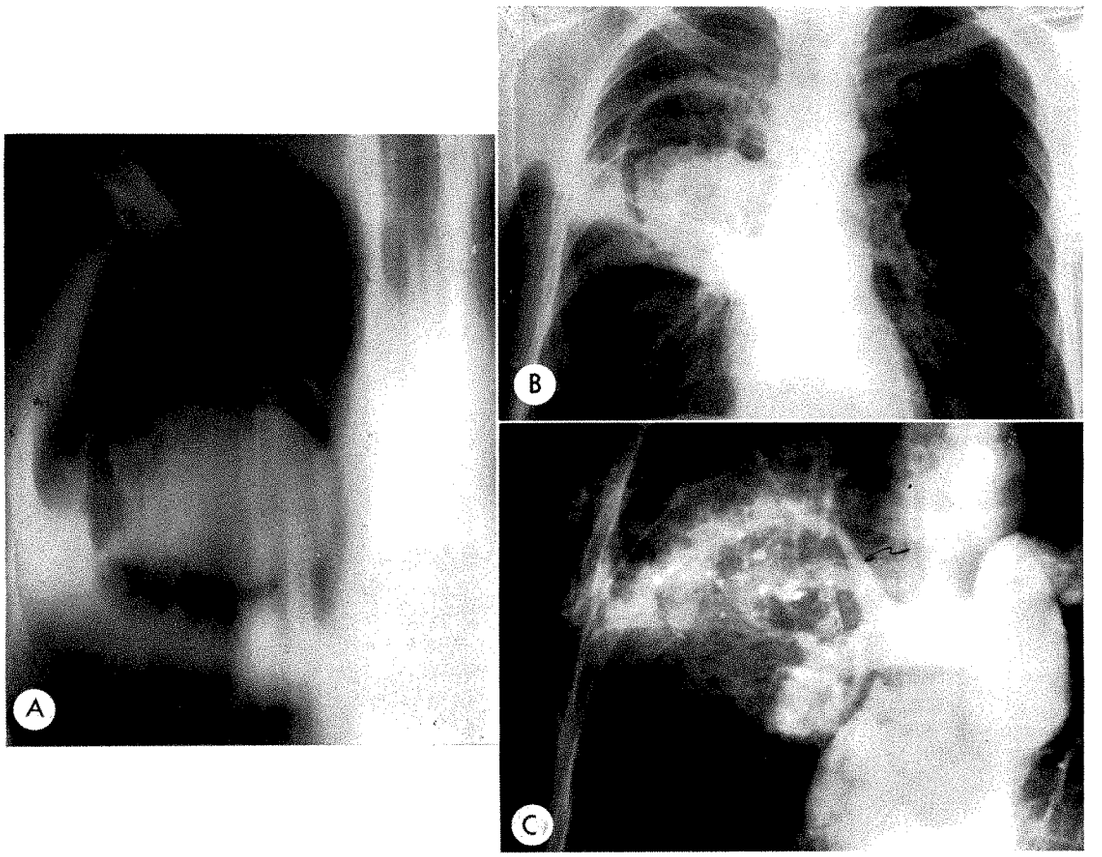


Fig. 5. (*A–C*) *Phycomycosis.* This 34 year old juvenile onset diabetic was admitted with fever and cough on March 24, 1969 with a right upper lobe infiltrate. (*A*) Two days later a tomogram disclosed a large cavity with a central mass lesion attached to the inner walls of the cavity. (*B*) One week later, the lesion had increased in size; however, an open lung biopsy and debridement failed to reveal the true diagnosis. (*C*) The pulmonary angiogram shows poor filling of the superior branches or the right pulmonary artery. On April 23, 1969, 6 days following *C*, the patient was dead, having exsanguinated from the mucor lesion eroding the pulmonary artery and extending through the right main stem bronchus. The histology was finally established at autopsy.

terminally a bronchopleural fistula developed.

In spite of the small number of cases, the aggressive tendencies of the Phycomycetes in 2 of the 3 cases allowed it to present a unique roentgenographic pattern with no significant opportunistic differential considerations.

IV. Cytomegalic inclusion disease (C.I.D.)

The 5 cases of C.I.D. were all noted in adults. The common roentgenologic features were poorly defined alveolar infiltrates, in all cases limited to the upper lung fields (Fig. 6). None of these lesions were observed to undergo excavation. With 1 exception, they tended to follow a less aggressive course than any of the opportunistic organisms we reviewed. This exception occurred in a 33 year old male renal transplant patient, whose lung disease progressed to a diffuse alveolar process over a 1 week period of time and represented the primary cause of his death. The principal roentgenographic differential considerations in this C.I.D. group thus concerned septic pulmonary emboli, aspergillosis and pulmonary lymphoma. None of

our 5 cases involved an individual with an underlying lymphoma.

V. ASPERGILLOSIS

All 4 of the cases of aspergillosis presented with an ill-defined nodular pattern usually confined to the upper lung fields. Each of these nodular lesions subsequently underwent excavation. In 2 cases with serial roentgenographic films available for review, the process of cavitation occurred within 5 days (Fig. 7, *A* and *B*). There were no examples of an alveolar lobar or segmental infiltrative pattern.

The principal differential roentgenologic consideration with aspergillosis should include septic pulmonary embolic episodes, to be described subsequently. Since the lesions initially presented as "shaggy nodules," the other components of that differential gamut should be mentioned, and include pulmonary lymphoma, Wegener's granulomatosis, terminal bronchiolar carcinoma and choriocarcinoma. The infrequency of excavation in pulmonary lymphoma, terminal bronchiolar carcinoma and choriocarcinoma allows these entities to be excluded (Fig. 8).

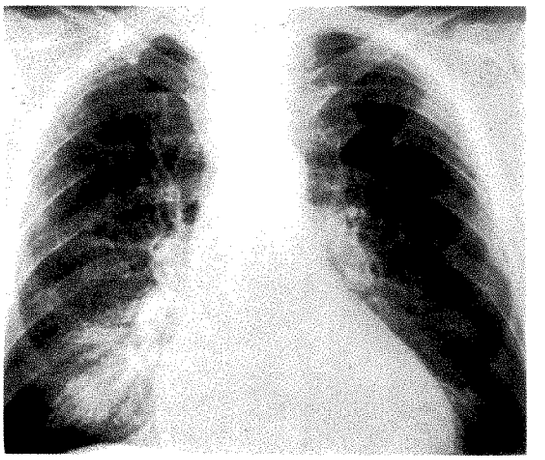


FIG. 6. *Cytomegalic Inclusion Disease (C.I.D.).* This 44 year old renal transplant patient developed a low grade temperature 5 days prior to this roentgenogram. Note the oval, 0.3–1.0 cm. nodular densities limited to both upper lung fields. The diagnosis of C.I.D. was proven at open lung biopsy 3 days later. The nodules cleared without treatment in 1 month.

VI. BACTERIAL INFECTION

Since many organisms were involved in this category of opportunistic lung disease, only the more frequently observed bacteria will be discussed. The staphylococcal

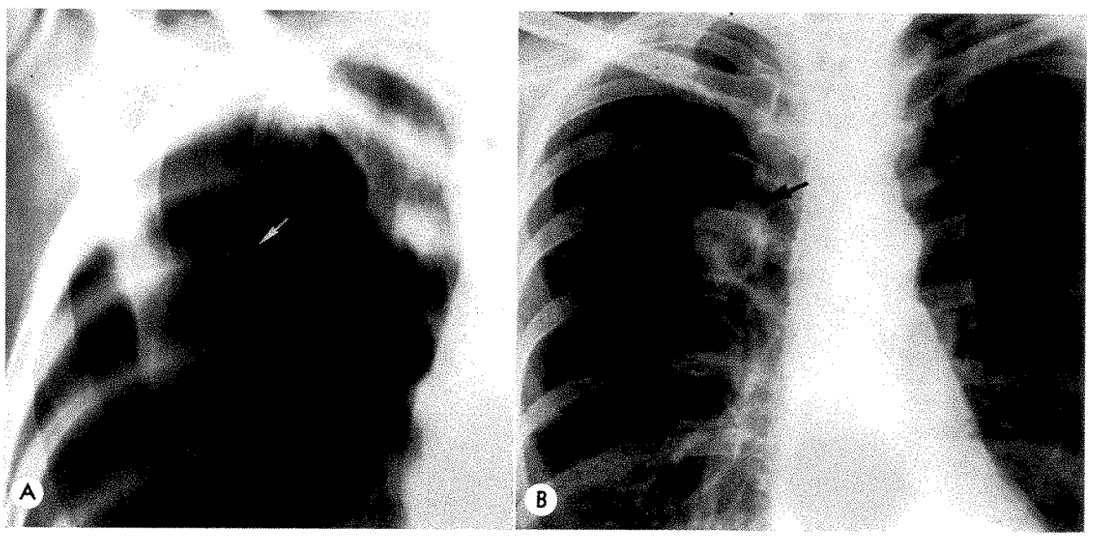


FIG. 7. (*A* and *B*) *Aspergillosis.* The initial roentgenogram on presentation of this 44 year old female renal transplant patient disclosed a well-defined right upper lobe mass. (*A*) Tomogram on August 6, 1969, revealed a solitary 1.5 cm. mass without cavitation (arrow). (*B*) Within 2 weeks, a second lesion appeared and rapidly excavated (arrows). On August 22, 1969, open thoracotomy revealed *Aspergillus fumigatus* in both nodules.

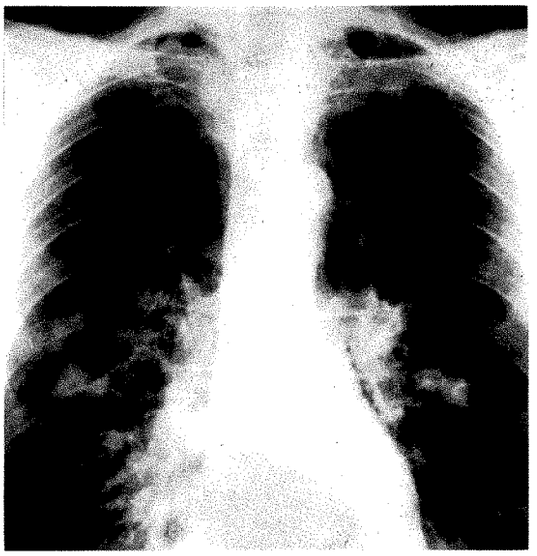


FIG. 8. *Lymphoma (lymphocytic).* The differential considerations of the "shaggy nodule" are: 1. septic emboli (*Staphylococcus, Pseudomonas*); 2. aspergillosis; 3. lymphoma; 4. Wegener's granulomatosis; 5. terminal bronchiolar carcinoma; 6. choriocarcinoma. In such a clinical setting, possibilities would include choices 1, 2 and 3. The presenting symptoms, course and lack of excavation make pulmonary lymphoma the primary choice.

group was responsible for 6 instances of infection. In 4 of the 6 cases, the roentgenograms reflected an embolic hematogeneous process, with fluffy nodular densities scattered throughout both lung fields. These commonly and rapidly underwent excavation to form lung abscesses (Fig. 9, *A* and *B*).

Four of the 6 episodes of Pseudomonas pneumonia developed consolidative lobar disease with expansion of the affected lung volume.[29] This roentgenographic feature, we feel, is specific for necrotizing gram negative bacterial pneumonias and most particularly the Pseudomonas organism. The only roentgenologic differential consideration should be that of a primary lung tumor, especially terminal bronchiolar carcinoma[12] (Fig. 10).

The remainder of the bacterial group reviewed in this series presented as an ordinary segmental or lobar pneumonia with no distinguishing characteristics roentgenologically. The presence of significant pleural effusion in bacterial opportunistic lung disease was an ominous sign, pointing toward the development of an empyema.[22]

No unique or specific roentgenologic findings were associated with the 2 cases of candidiasis or the single case of coccidioidomycosis.

SUMMARY

Fifty-two instances of opportunistic lung disease were reviewed with regard to

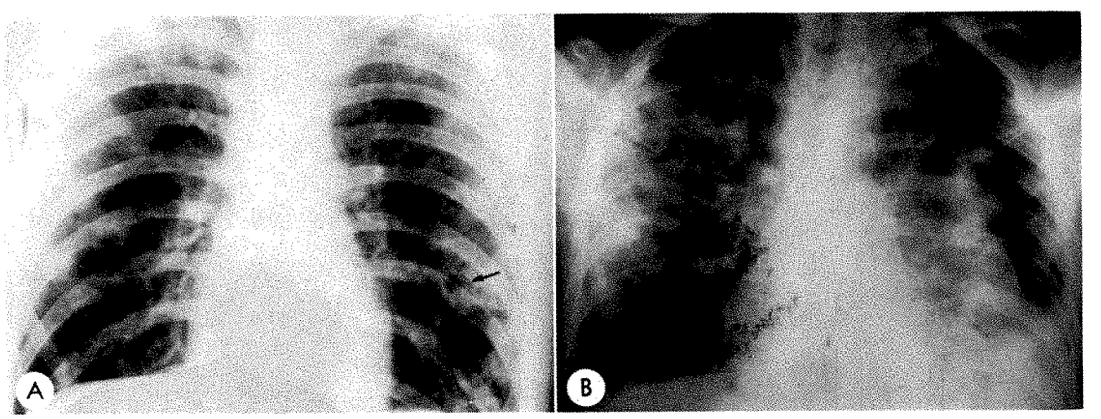


FIG. 9. (*A* and *B*) *Staphylococcal Pneumonia.* This 13 year old male, on high dose steroids for a brief period, apparently coincident with the onset of signs of meningitis, developed pulmonary symptoms on September 13, 1972. (*A*) Roentgenogram made on September 14, 1972 shows the ill-defined nodular infiltrates, "shaggy nodules," 2 of which have already undergone excavation (arrows). (*B*) Roentgenogram made on September 19, 1972, already shows a pyopneumothorax. Note the extensive progression of the hematogeneous staphylococcal pneumonia throughout both lung fields.

their roentgenologic presentation and course. Familiarity with the underlying disease and its therapy must be brought into focus with an understanding of the differing patterns of opportunistic lung disease both clinically and roentgenologically.

Emphasis should be placed on the alveolar nature of *Pneumocystis carinii* pneumonia rather than the previously described interstitial, perihilar roentgenographic pattern. In its florid presentation, diffuse alveolar opacification of the lung fields is the hallmark of this disease roentgenologically.

Nocardiosis should be suggested by an infiltrative or nodular lesion with cavitation, particularly in a patient having undergone transplantation and subsequent immune suppression.

The aggressive tendencies of the *Phycomycetes* in a small group of patients were characterized by fistula formation, vascular and tracheobronchial invasion.

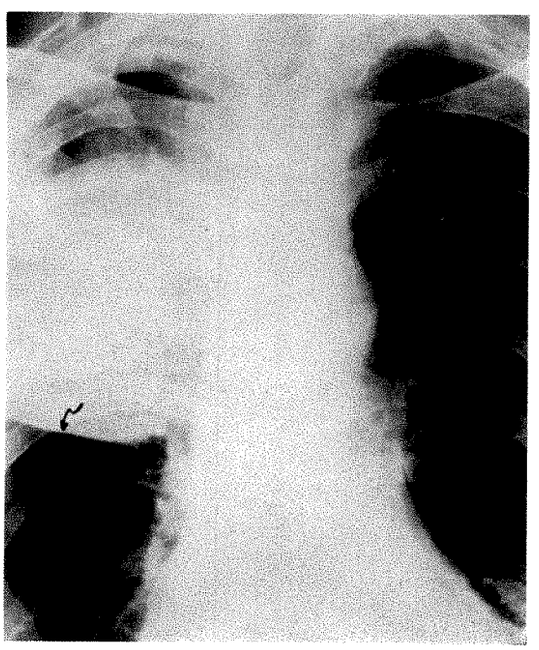


FIG. 10. *Pseudomonas Pneumonia.* The differential considerations of an infiltrate showing lobar expansion are: 1. necrotizing bacterial pneumonia (*Pseudomonas, Klebsiella, Staphylococcus*); 2. tumor (terminal bronchiolar carcinoma). The clinical setting should easily separate these 2 differential problems.

By comparison, the benign ill-defined nodular infiltrates of cytomegalovirus infection formed a striking contrast, with a propensity for upper lobe distribution.

Aspergillosis should be suggested by a "shaggy nodule" appearance which rapidly excavates.

The broad group of bacterial organisms could be suggested by the nodular embolic form of the disease, more commonly seen with staphylococcal pneumonia as well as pneumonia with lobar expansion, seen with the gram negative organisms.

Knowledge of the above presenting roentgenologic patterns and an awareness of the frequency of opportunistic disease should enhance our diagnostic accuracy and lead to earlier and more aggressive methods of diagnosis and treatment.

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ROENTGENOGRAPHIC FINDINGS IN PULMONARY MUCORMYCOSIS*

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FUNGI of the order *Mucorales* (mucormycosis or phycomycosis) are generally considered saprophytic and not pathologic in man. In the face of pre-existing disease, however, mucormycosis may become a serious and usually fatal invader. The common sites of infection are the sinuses and cerebral venous structures, although involvement of every organ system has been reported.[8,18] The fungus has a predilection for vascular structures and thrombosis in involved areas is almost universal. Pulmonary involvement with *Mucor* has been quite uncommon, but the incidence has been increasingly recognized, especially in patients with leukemia, lymphoma, or diabetes. Between 1968 and 1972, 6 fatal cases have been observed at the Peter Bent Brigham Hospital.

REPORT OF CASES

Case I. S.E. (15-61-01), an 18 year old white female with acute lymphoblastic leukemia, had received vincristine, prednisone, cytosine arabinoside, and daunomycin during the 5 months preceding her final admission. On her last admission she was complaining of cough and generalized weakness with a fever of 103°F. The initial chest roentgenogram showed consolidation of the right upper lobe and elevation of the right hemidiaphragm (Fig. 1*A*). No effusions were present. Her white blood cell count was 700/mm.^{3} *Escherichia coli* was cultured from the blood. Her pneumonia progressed rapidly despite antibiotics and transfusions, and she died 5 days after admission. A chest roentgenogram shortly before death showed consolidation with cavitation of the right upper lobe and patchy infiltrates in both the left upper and left lower lobes (Fig. 1*B*).

Autopsy revealed severe bilateral bronchopneumonia with multiple small infarcts and a large abscess in the right upper lobe. Microscopic sections showed Mucorales species throughout the lung.

Case II. G.D. (11-21-52), a 69 year old white female, had chronic myelogenous leukemia diagnosed 3 years previously. She had received leukeran, myeleran, cytosine arabinoside, thioguanine and splenic irradiation. For the 10 months preceding her final admission she was in blast crisis. She was admitted because of deteriorating mental status, severe generalized

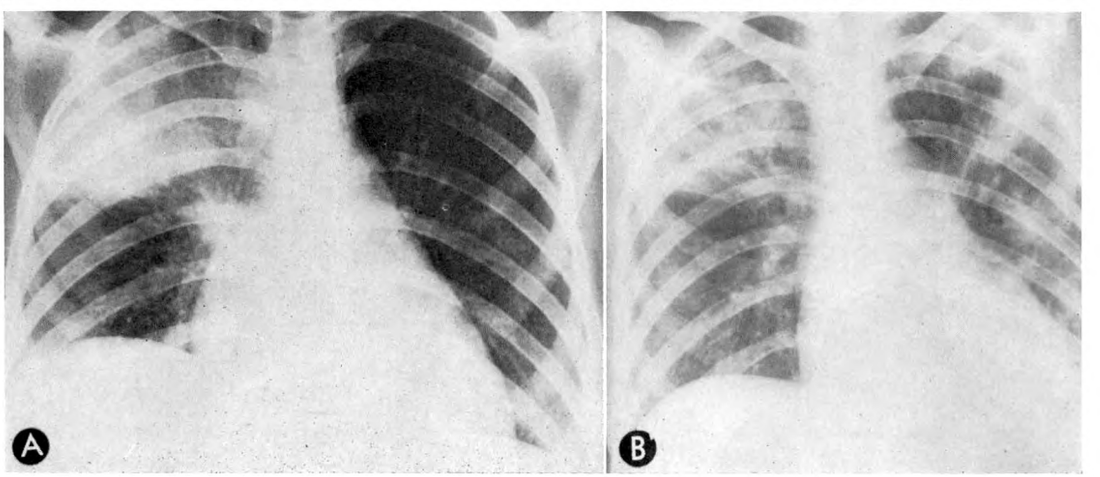


Fig. 1. Case I. (*A*) Consolidation is visible in the right upper lobe. (*B*) Eleven days later patchy infiltrates are evident in the left lung, and there is cavitation in the right upper lobe.

* From the Department of Radiology at Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts. Supported in part by USPHS grants GM01910 and GM18674.

weakness, and low grade fever. Her only respiratory complaint was mild cough with occasional hemoptysis. The chest roentgenogram showed cardiomegaly with mild congestive heart failure. In addition there was an ill-defined 8 mm. nodule in the left upper lobe which had not been present on earlier roentgenograms (Fig. 2). She developed rectal bleeding on the first day and died on the third hospital day.

Autopsy revealed 3 small hemorrhagic lung infarcts in the right upper, left upper, and left lower lobes. *Mucorales* species were present in these areas as well as in several large splenic infarcts. There were also several large ulcers in the colon, but no fungus could be found.

Case III. E.S. (16-01-52), a 43 year old white male, had Hodgkin's disease diagnosed 4 months prior to death. He received methotrexate, vincristine, prednisone, and procarbazine chemotherapy and was clinically well until developing a cough, chest pain, and high fever. A chest roentgenogram showed bilateral lower lobe consolidations (Fig. 3*A*). He was admitted and a percutaneous needle biopsy revealed hyphae. He was treated with bleomycin, gentamicin, amphotericin B, and pentamidine. Cultures were negative. Despite therapy his condition deteriorated markedly for 2 weeks. Serial chest roentgenograms showed progression of infiltrates into both upper lobes and increasing consolidation. One day before death a large right pleural effusion developed (Fig. 3*B*).



Fig. 2. Case II. The poorly circumscribed density in the left upper lobe (arrow) subsequently proved to be a hemorrhagic infarct containing *mucorales* species.

Autopsy showed a large right hemothorax. There was massive consolidation and necrosis of both lower lobes and multiple small focal

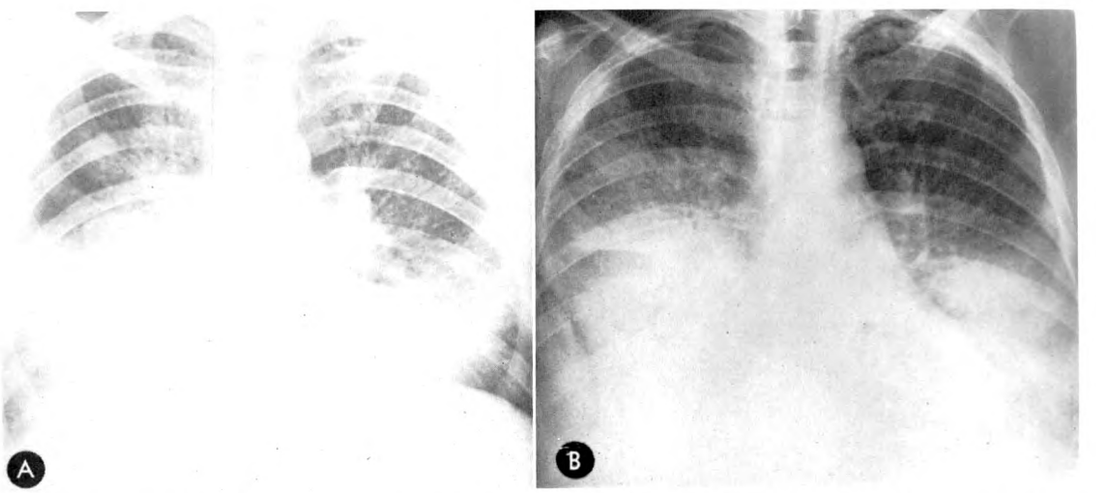


Fig. 3. Case III. (*A*) Admission roentgenogram shows bilateral lower lobe infiltrates. (*B*) Progression of the lower lobe infiltrates and a large right pleural effusion are apparent.

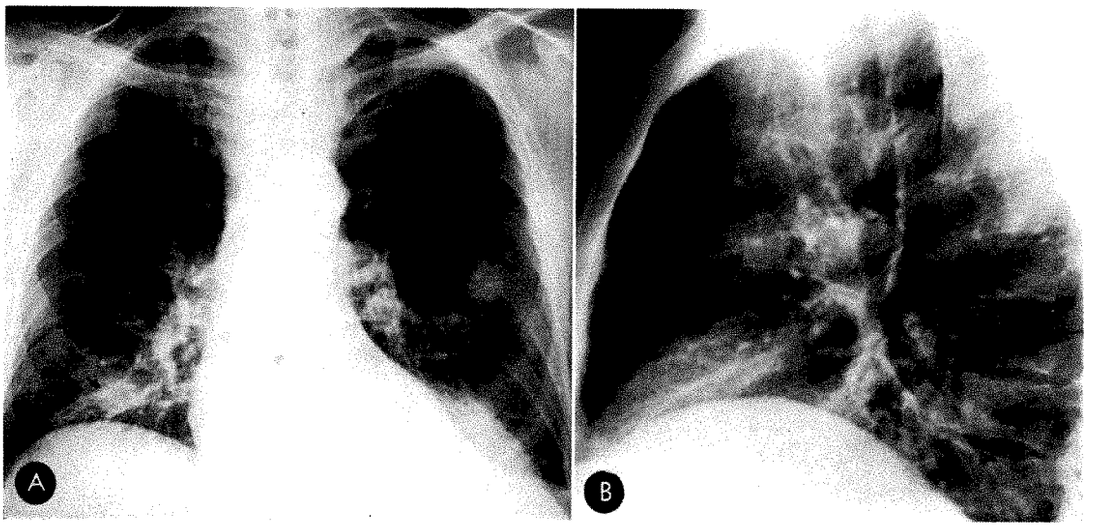


FIG. 4. Case IV. (*A*) Anteroposterior roentgenogram. Arrows indicate cavitating lesions in the left upper lobe and the right lower lobe. (*B*) Lateral roentgenogram. Arrows indicate same lesions as seen in *A*.

infarcts and infiltrates in the upper lobes. Microscopic sections contained massive numbers of *Mucorales*.

CASE IV. H.B. (10-00-93) was a 57 year old white male with chronic lymphocytic leukemia for 3 years. He had received cytoxan, vincristine, prednisone, decadron, methotrexate, and L-aspariginase. He was admitted because of sudden obtundation. A chest roentgenogram showed a small left pleural effusion and two 2.5 cm. cavitating lesions, one in the left upper lobe and the other in the right lower lobe (Fig. 4, *A* and *B*). He died on the second hospital day.

Autopsy revealed a large intracerebral hematoma as an immediate cause of death. In addition there were two 2 cm. abscesses in the left upper and right lower lobes. Microscopic sections showed both abscesses to be full of *Mucorales*.

CASE V. M.B. (10-34-28), a 37 year old white female with acute myelogenous leukemia, had been treated with cytoxan, methotrexate, dactinomycin, vincristine, and prednisone. She was admitted for urinary retention and fever evaluation. A chest roentgenogram showed an infiltrate in the right apex and a soft tissue mass adjacent to sternum. Sputum and blood cultures were negative. *E. coli* was cultured in the urine. Her fever continued and her clinical and mental status worsened. A chest roentgenogram 4 days before death showed slight progression of the right upper lobe infiltrate. There were no cavities or consolidation. On the 18th hospital day, multiple hemorrhagic diathesis developed and the patient died.

Autopsy showed infarction of the left lower lobe with diffuse bronchopneumonia of all lobes. There were multiple focal infarctions and hemorrhage in the right upper lobe. Microscopic sections contained *Mucorales*.

CASE VI. M.B. (15-81-57) was a 53 year old white female, who developed idiopathic aplastic anemia 3 months prior to death. She was treated with oxymethalone and prednisone but had no response. She was admitted for the final time because of fever, low back pain and nausea. Admission chest roentgenogram showed a left lower lobe infiltrate which cleared after 2 weeks of antibiotic therapy. Eighteen days after admission her chest was clear roentgenologically, but her clinical condition had continued to deteriorate. She received 2 bone marrow transplants with mild febrile and hemolytic reactions. Two days after the final transplant, she developed a fever with rapidly increasing respiratory insufficiency. Her white blood cell count was 700/mm.^{3} with no granulocytes. Chest roentgenogram showed diffuse infiltrates in all portions of the lung with consolidation of the lingula and right middle lobe. Blood cultures grew gram-negative rods. Her condition deteriorated rapidly and she died 48 hours later.

Autopsy showed extensive hemorrhage in the

lung with multiple colonies of *Pseudomonas* and *Enterobacter*. The lingula and pericardium were extensively involved with colonies of *Mucorales* which were invading the vascular channels.

DISCUSSION

The term mucormycosis has been used in the literature to refer to infection by any member of the order *Mucorales*. In man 3 genera of *Mucorales*, *Mucor*, *Absidia*, and *Rhizopus*, have been definitely implicated as opportunistic pathogens. All of these fungi belong to the class *Phycomycetes*, and the term phycomycosis has been used by some authors to describe the infections. Differentiation of the 3 genera can only be determined from cultures.[28]

Since the first case of pulmonary mucormycosis was described by Paltauf in 1885,[31] there have been 69 cases reported in the English language literature.[1,4,9,13,20,23,25,27,39,41] In 62 of these an underlying disease was associated. There is only 1 definite case of the infection occurring in an otherwise healthy individual.[2] A report of an asymptomatic 4 cm. mycelioma due to *Mucor*[30] has been considered by a subsequent review of the pathology to be not adequately identified as *Mucorales*.[38]

The most common predisposing condition was leukemia which was present in 36 cases. Diabetes mellitus was found in 14; Hodgkin's disease in 2; and severe uremia in 2.[24,36] The following predisposing conditions were represented by single case reports: Cushing's disease,[35] infantile diarrhea,[26] massive antibiotic treatment for otitis media,[18] agammaglobulinemia,[7] severe burns,[2] overwhelming sepsis,[28] bronchogenic carcinoma,[38] acute hepatic necrosis,[28] and carcinoma of the pancreas.[38]

In 38 reports which specified sex, 28 were males. The age range was 16 days to 72 years. Pathologic findings were given for 21 cases. All of these cases had pulmonary vascular thrombosis and infarction of varying degrees. Large infarcts with cavitation were present in 6 of these cases. In 1 case there was a bronchopleural fistula. Of the 69 patients only 4 survived the infection.

The pathophysiology underlying infection by *Mucorales* is not clear. Spores are ubiquitous and are frequently inhaled by most of the population. *Mucor* is frequently grown in throat cultures, but tissue invasion is rare. Impaired white blood cell function can give rise to clinical infection, but even in the presence of leukemia the disease is uncommon. Baker *et al.*[3] found that laboratory animals on high doses of steroids were more susceptible to infection. Elder and Baker[12] showed that rabbits made diabetic with alloxan developed pulmonary lesions from inhaled spores during the acute phase of the diabetes but were resistant during the chronic phase. The degree of hyperglycemia did not influence the infection, and they considered ketosis or acidosis the probable pathophysiologic mechanism. Bauer *et al.*[5] found, however, that hyperglycemia was a predisposing condition in rabbits. At the present time it is not possible to clearly define the alterations in normal body function which permit the fungus to grow or to explain its preference for blood vessels. It can merely be added to the growing list of opportunistic invaders.

Several authors have reported on the incidence of mucormycosis pneumonia in opportunistic pulmonary infections.[19,21,22,32,33,36] In general, it was an uncommon invader varying in frequency from 1 in 39 cases to a high of 6 in 14. In all these series *Candida* species were the most common pathogens with aspergillosis ranking second in all but 1.

No treatment has been very effective. Of the 4 reported survivors, 2 were treated with pulmonary lobectomy[6,11] and 2 with amphotericin B.[7,29]

The 6 cases reported here follow the predisposition patterns cited in previous reports. Four of the 6 had leukemia, a fifth had Hodgkin's disease and was severely leukopenic, and the sixth had aplastic anemia with no circulating granulocytes. All died, and all had areas of pulmonary vascular thrombosis and infarction.

CHEST ROENTGEN FINDINGS

There have been 13 cases of pulmonary mucormycosis reported in which chest

roentgen findings were described.[2,3,6,7,10,24,29,34,35,37,40] In 1 of these the chest roentgenogram was reported as "normal;" at autopsy, however, a 5 cm. lung abscess was found, making it likely that the roentgenogram was taken quite some time before death.[2] In the remaining 12 cases the lungs were described as having an infiltrate in 5, a patchy or nonhomogeneous infiltrate in 4, and a consolidation in 3. In addition, 4 readings mentioned a cavity and 1 noted a pleural effusion. The distribution of lesions was fairly random with the right and left lower lobes involved in 4 cases each, the right upper lobe in 3, and the left upper lobe in 2. Only 5 of the 12 cases described had more than 1 lobe involved, but some reports had been edited and it is likely that the incidence of multiple lobe involvement was higher.

Our 6 cases reaffirm the lack of specific roentgen findings in *Mucorales* pneumonia. Five of the 6 cases had consolidation, 1 case had only a nonspecific infiltrate. There was no definite lobar predilection, with the various lobes all having similar representation. Effusion was present in only 1 of the present cases. Two patients had cavitating infiltrates, and 1 patient had a small parenchymal nodule.

CONCLUSIONS

There are no definitive roentgen criteria for diagnosing pulmonary mucormycosis, but the radiologist should be aware of the clinical setting for opportunistic infection, because certain clues on the chest roentgenogram may then enable him to suggest *Mucorales* as the causative agent. Pleural effusion is not common. There is no tendency for peripheral lung field sparing as is common with *Pneumocystis* infection.[15] Over half the cases have nonhomogeneous densities in the lung fields. The universal pulmonary infarcts undoubtedly account for this and for the frequent appearance of cavitation. Such cavitation can also occur in candidiasis and aspergillosis, and roentgen differentiation from these organisms is probably not possible.[14,16] The presence of multiple consolidations with or without a cavity, however, should suggest the possibility of a fungal rather than a bacterial or parasitic etiology.

SUMMARY

Patients with leukemia or diabetes mellitus are especially predisposed to pulmonary mucormycosis.

The lack of pleural effusion, and peripheral lung involvement, inhomogeneous densities, and consolidations with cavitations on the chest roentgenogram are suggestive of fungal infection. Lung biopsy will establish a definitive diagnosis.

Differentiation between mucormycosis, candidiasis and aspergillosis is not possible roentgenologically.

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BRONCHIOLITIS OBLITERANS*

ROENTGENOLOGIC-PATHOLOGIC CORRELATION

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BRONCHIOLITIS obliterans is an end result of lower respiratory tract damage, in which bronchioles become obstructed by organizing exudate and polypoid masses of granulation tissue. Behind the obstructed bronchioles, fat-filled phagocytes may accumulate, forming an "obstructive," "golden," or "cholesterol" pneumonitis. In other cases, air-trapping predominates. Early roentgenographic recognition of this process may be invaluable to the patient, permitting diagnosis and treatment before irreversible changes develop.

The first reference to bronchiolitis obliterans was made by Reynaud in 1835.[26] It was not mentioned again in medical writings until 1901, when Lange[13] described 2 fatal cases of unknown origin. Since that time it has been described following toxic inhalations (war gas,[29] nitric, hydrochloric or sulfuric acid fumes,[3,14,18,22,24] talcum powder,[19] zinc stearate,[10] hot gases[23]), as a consequence of respiratory infections (including influenza,[30] measles,[5] whooping cough,[5] and adenovirus 21[4]) and also following inhalation of foreign bodies.[5] Microscopic descriptions of bronchiolitis obliterans have mentioned both the polypoid appearance of the organizing exudate[11,16,20] and also complete occlusion of the lumen with the final appearance of the bronchiole as a fibrous scar.[14,16,17,20] The surrounding parenchyma has sometimes been noted to be involved with an obstructive pneumonitis.[8] In other cases, surrounding zones of emphysematous alveoli have been described and attributed to bronchiolar obstruction with collateral ventilation.[6,25] These changes have been experimentally produced in dogs by exposure to chlorine,[29] phosgene,[29] and zinc stearate.[10] Intratracheal injection of nitric acid has produced the lesion in rabbits.[20] Some beneficial effect from steroids has been shown in animal experiments.[20] Improvement with steroid treatment in humans has been documented in silo-filler's disease.[14,21] Steroids have also been used in combination with other modes of treatment in patients recovering from bronchiolitis obliterans due to inhalation of hot gases[23] and also infectious disease.[9]

In the literature, many different roentgenographic appearances have been attributed to bronchiolitis obliterans. In the earliest reports, the pattern was usually described as miliary.[2,5,12] Cases secondary to known toxic inhalations generally showed a pattern suggesting pulmonary edema,[23,24] occasionally with zones of discrete nodularity. More recently, attention has been directed toward unilateral or bilateral hyperinflation, associated also with cylindrical or saccular bronchiectasis.[4,7] Cases with linear densities,[9] atelectasis,[9] granular and reticular infiltrates,[9] diffuse nodular patterns,[9] patchy bronchopneumonia[4] or lobar involvement[1] have been reported.

MATERIAL

We reviewed all consultation cases filed under the diagnosis of bronchiolitis obliterans, bronchiolitis obliterans with interstitial pneumonia, chronic bronchiolitis, and cholesterol pneumonia. Of these, approximately 80 were selected as showing a major component of bronchiolitis obliterans on pathologic examination of surgical or

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Table I

SEX DISTRIBUTION

Male	Female	Total
34 (65%)	18 (35%)	52

AGE DISTRIBUTION

Less than 20 years	7	Range: 10 mo.–75 yr.
20–39	5	80% of patients were
40–59	26	over 40 yr.
Over 60 years	14	

autopsy material. We were able to obtain original roentgenograms or reproductions in 52 cases. These form the material for the clinical and roentgenologic analysis which follows. We are very much indebted to the physicians and radiologists who made roentgenograms and follow-up information available to us.

CLINICAL FEATURES

Sixty-five per cent of the patients were males. The age distribution ranged from 10 months to 75 years, with 80 per cent (41) over 40 years of age (Table I). Onset was generally insidious, extending over a period of several weeks. The disease was treated empirically, on the average for an additional 2–3 months before biopsy and diagnosis. Only 1 patient was asymptomatic when the lesions were discovered roentgenologically. The most common clinical finding was cough, recorded in 39 out of 41 cases with adequate history. The next most common manifestation was dyspnea, which was specifically commented on in 36 out of 40 cases. Sputum production (25/32) and fever (22/35) were also frequent presenting signs. Rales were noted in 30 out of 36 cases with documented physical findings (Tables II and V). In 18 patients, the lesions of bronchiolitis obliterans appeared to be residual from an incompletely resolved pneumonia, but in 34 others, new or recurrent disease was indicated by clinical or roentgenologic findings. Surprisingly, only 11 patients had a history of chronic bronchitis or recurrent respiratory tract infection, including 3 asthmatics. Eight had histories of toxic inhalational exposure, including 3 cases of aspiration and 1 of acute exposure to nitric acid fumes (Table III). Ten patients had serious co-existing diseases, such as uremia, lymphoma or leukemia; or collagen diseases such as idiopathic thrombocytopenic purpura, rheumatoid arthritis or scleroderma (Table IV).

Table II

SYMPTOMS

	Yes	No	Not Reported
Cough	39 (95%)	2	11
Dyspnea	36 (90%)	4	12
Sputum	25 (78%)	7	20
Malaise	18 (100%)	—	34

Table III

PATHOGENESIS

Post-pneumonic	18
Chronic pulmonary infection	11 (3 with asthma)
Toxic inhalation	8 (3 with aspiration)
Unknown etiology	21
Total	58 (several patients with more than one known etiology)

Laboratory findings were abnormal in many cases, but generally as nonspecific as the clinical findings. The white blood cell count was elevated above 10,000 per cu. mm. in 26 out of 41 cases. Bacterial or fungal culture of sputum was positive for respiratory pathogens in 14 out of 37 re-

Table IV

COEXISTING DISEASES

Congestive heart failure	2
Lymphoma	2 (1 with idiopathic thrombocytopenic purpura, 1 with diabetes)
Acute lymphocytic leukemia	1
Pulmonary alveolar proteinosis	1
Chronic glomerulonephritis (renal failure)	1
Scleroderma	1
Myasthenia gravis	1
Rheumatoid arthritis	1

TABLE V

CLINICAL FINDINGS

	Yes	No	Not Reported
Fever	22	13	17
Rales	30	7	15
White blood cells more than 10,000/mm.^{3}	26	15	11
Positive sputum	14	23	15

(6 *D. pneumoniae*, 2 *Candida*, 2 *Klebsiella*, 2 *Pseudomonas*, 1 *Staphylococcus*, 1 atypical AFB)

PULMONARY FUNCTION TESTS

Restrictive	Obstructive	Normal	Not Reported
9	7	6	29

ports. Eosinophilia (over 5 per cent) was noted in only 3 cases. Viral studies were rarely reported; none of these was positive. Pulmonary function data were available in 22 patients; a restrictive pattern was demonstrated in 9, and obstructive findings were noted in 7. Six patients had normal studies (Table v).

ROENTGENOLOGIC FINDINGS

For purposes of classification, we have divided the roentgenologic findings into 3 main groups: *nodular densities* (18 cases); *alveolar opacities* (39 cases); and *hyperinflation* (2 cases). Several cases exhibited more than 1 of these patterns at different stages of the disease, and have been counted twice (Table VI).

TABLE VI

ROENTGENOLOGIC CLASSIFICATION

I. Nodular Densities (18 cases)
  a. Micronodular (less than 0.5 cm.) (5 cases)
  b. Discrete nodular (more than 0.5 cm.) (5 cases)
  c. Confluent nodular (6 cases)
  d. Lineonodular (5 cases)
II. Alveolar Opacities (39 cases)
  a. Bibasilar (10 cases)
    1. Diffuse (edema-like) (2 cases)
    2. Linear (atelectatic) (2 cases)
    3. Mixed (honeycomb) (6 cases)
  b. Other locations (29 cases)
    1. Lobar or segmental (20 cases)
    2. Diffuse (edema-like) (2 cases)
    3. Multiple irregular opacities (8 cases)
III. Hyperinflation (2 cases)

Lobar or Segmental Distribution (bibasilar excluded) (20 cases)

Right upper lobe	10	Left upper lobe	3
Right middle lobe	7	Left lower lobe	3
Right lower lobe	6		

Nodular densities were subdivided into *micronodular* (distinct densities less than

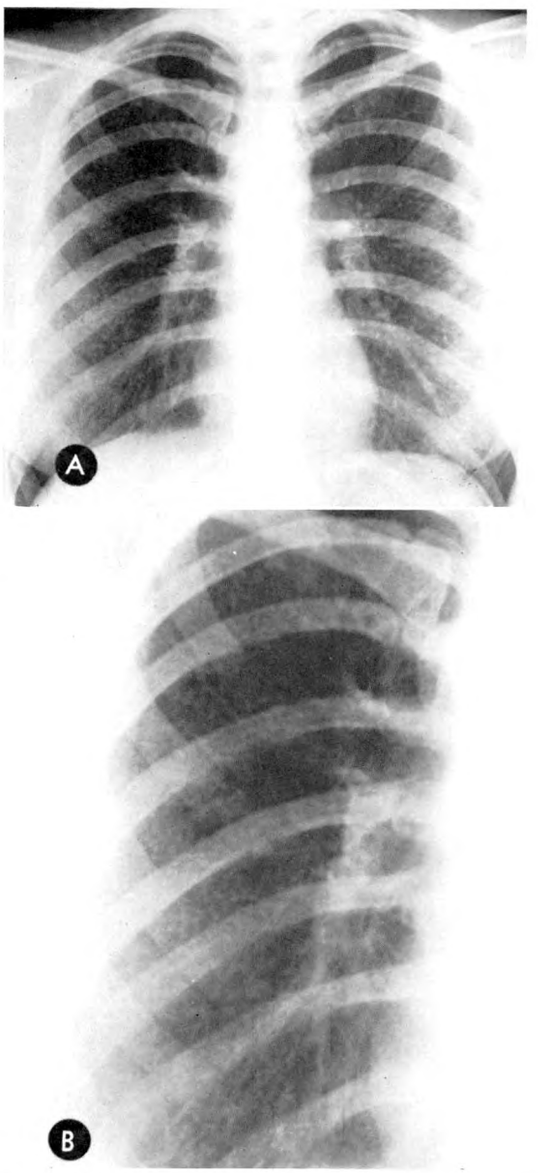


FIG. 1. (*A*) Posteroanterior (PA) roentgenogram of the chest. Micronodular pattern; 18 year old female. Dyspnea for 1 month. (*B*) Detail, same patient.

0.5 cm. in diameter [5 cases]) (Fig. 1, *A* and *B*); *discrete nodular* (distinct densities greater than 0.5 cm. in diameter [5 cases]) (Fig. 2); *confluent nodular* (consolidations with a nodular pattern visible in less involved peripheral regions [6 cases]) (Fig. 3, *A* and *B*); and *lineonodular* (fine linear or reticular markings in addition to micronodular densities [5 cases]) (Fig. 4).

The *alveolar opacities* included varying degrees of atelectasis or consolidation, both subsegmental and lobar, sometimes with patchy involvement of both lungs. Of these, 10 cases had predominantly *bibasilar* involvement: *diffuse* (2 cases) (Fig. 5), *linear* (2 cases) (Fig. 6), or *mixed* forms, including reticular or honeycomb patterns, (6 cases) (Fig. 7). The remaining 29 cases included a preponderance of *segmental* or *lobar* consolidation and atelectasis (20 cases) (Fig. 8). The distribution, not counting the bilateral basilar group, included 10 cases with *right* upper lobe involvement, 7 with *right* middle lobe and 6 with *right* lower lobe findings, but only 3 with *left* upper lobe and 3 others with *left* lower lobe disease. Ten other cases of alveolar opacity were divided into: 2 with diffuse alveolar opacification like central pulmonary edema (Fig. 9); and 8 with multiple irregular opacities (Fig. 10, *A* and *B*). These included a mixture of shadows which individually varied from irregular nodules to segmental consolidation; some were unchanged on serial roentgenograms, while in other cases the irregular densities disappeared and re-appeared in different places (Fig. 10, *A* and *B*; and 18, *A–C*).

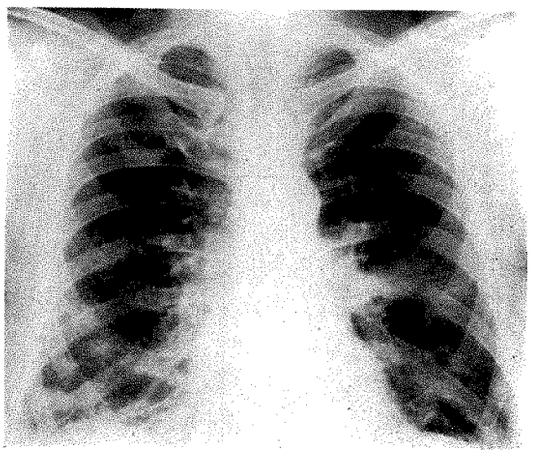


Fig. 2. PA chest. Discrete nodular pattern; 45 year old male. Cough and sputum for 4 months.

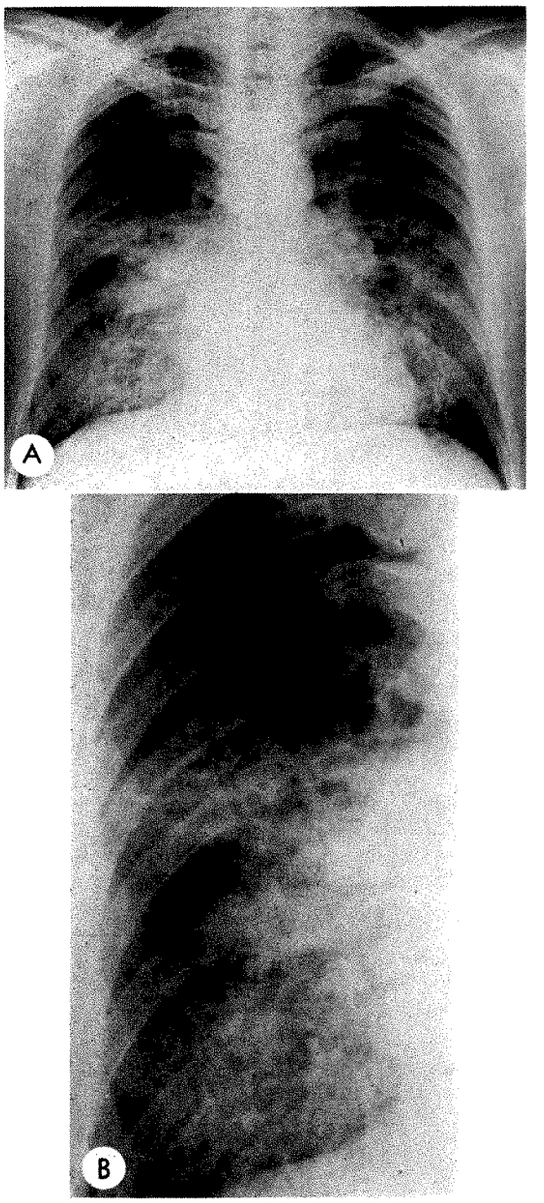


Fig. 3. (*A*) PA chest. Confluent nodular pattern; 49 year old male. Cough, fever, sputum for 2 months. (*B*) Detail, same patient.

Hyperinflation was noted in 2 children (Fig. 11, *A* and *B*), in 1 of whom it later disappeared; the hyperinflation of preexisting emphysema was excluded from

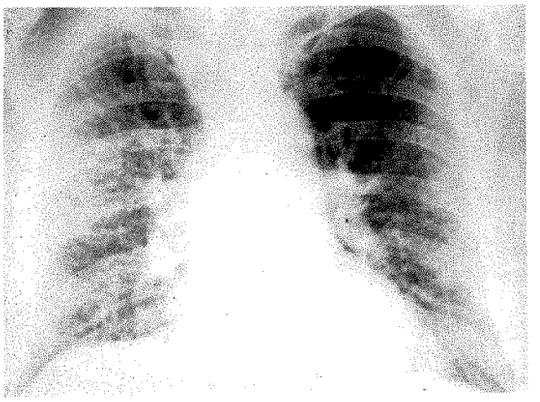


Fig. 4. PA chest. Lineonodular pattern; 65 year old male. Fever for "several weeks."

this category. In only 1 case was hilar lymphadenopathy identified: a child with chronic pulmonary infection.

Additional diagnostic roentgenographic procedures, such as tomography, bronchography, arteriography, or lung scanning were rarely employed in our series of patients. Useful additional information was not provided by these studies, when they were available.

Bronchiectasis was not a prominent feature in those cases in which it was sought bronchographically; there was cylindrical bronchial dilatation demonstrated in 1 case of segmental disease; in addition, several cases showed bronchiolectasis pathologically.

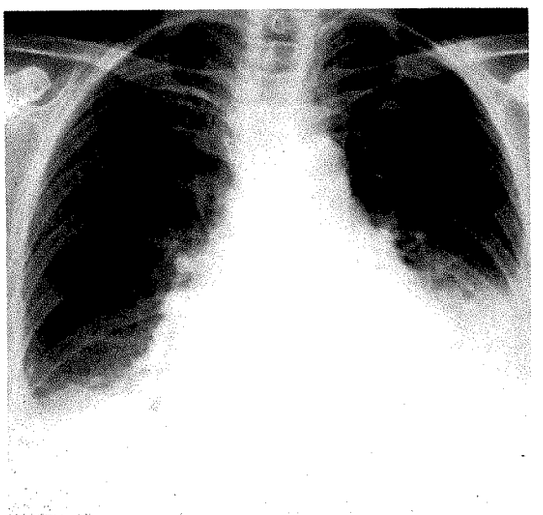


Fig. 5. PA chest. Diffuse bibasilar pattern; 71 year old female. Dyspnea for several months.

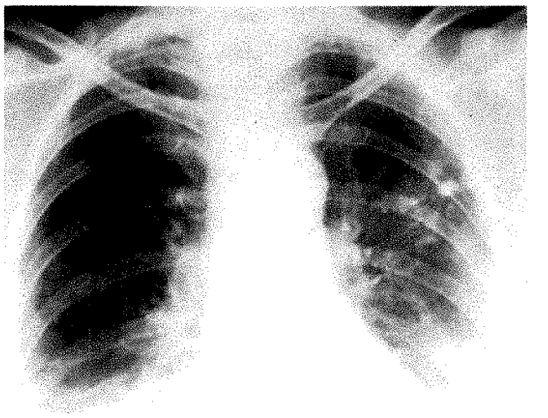


Fig. 6. PA chest. Linear bibasilar pattern; 50 year old female. Fever, cough and malaise for 4 months.

Roentgenologic Differential Diagnosis

Some of the patterns were clearly more distinctive than others. The *micronodular* and *lineonodular* patterns were similar to those in diffuse infectious granulomatous disease or occupational lung disease, or possibly pulmonary sarcoidosis. In bronchiolitis obliterans the nodules were less distinct than in most cases of these dis-



Fig. 7. PA chest. Mixed bibasilar pattern; 53 year old female. Cough, dyspnea and malaise for 4 months.

eases. The *discrete* and *confluent nodular* densities suggested other less common diseases, such as diffuse or localized vasculitis, multiple abscesses due to necrotizing pneumonia or sepsis, or carcinomatosis, either disseminated bronchiolo-alveolar cell carcinoma or metastatic. The *basilar opacities* were suggestive of chronic interstitial pneumonia, and this indeed may have coexisted in some cases. The roentgenologic findings in most cases, however, suggested only chronic or recurrent pneumonia and atelectasis, with aspiration an important possibility. These were manifest as *segmental* or *lobar* consolidation or atelectasis. Unilateral hyperinflation or "unilateral hyperlucent lung" (Swyer-James[28] or MacLeod's[15] syndrome) is usually diagnosed without difficulty by both radiologist and clinician, so that such patients rarely come to biopsy. This may account for the small number of cases with hyperinflation in our series.

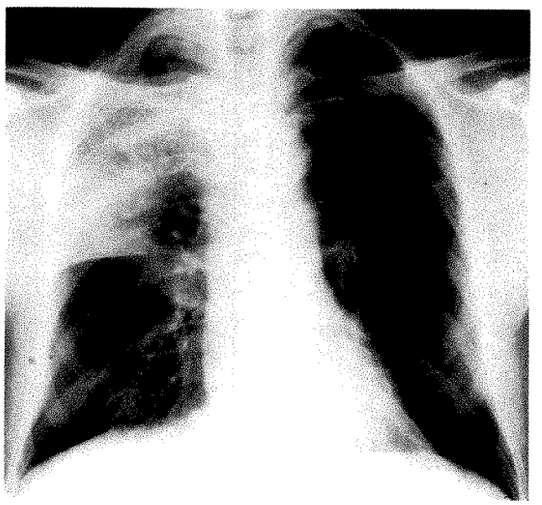


Fig. 8. PA chest. Lobar consolidation pattern; 64 year old male. Proven hiatal hernia with aspiration. (See also Fig. 20.)

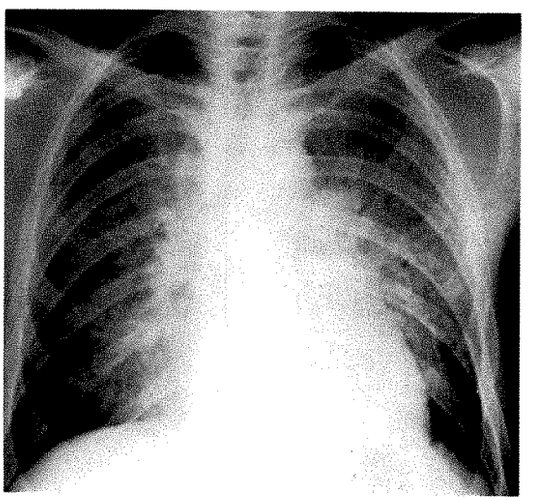


Fig. 9. PA chest. Diffuse alveolar opacity pattern; 26 year old male. Uremia with 2 week history of fever, cough, dyspnea, malaise. (See also Fig. 19.)

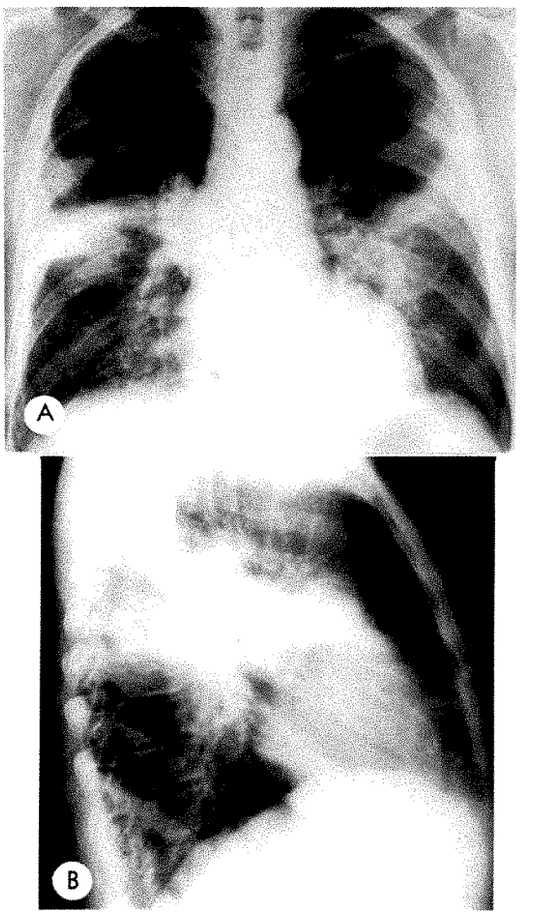


Fig. 10. (*A*) PA chest. Multiple irregular opacity pattern; 68 year old male. Recent onset of cough, sputum, dyspnea, malaise. (*B*) Lateral, same patient. (See also Fig. 18.)

PATHOLOGIC FINDINGS

The diagnosis was established as a result of surgical biopsy in 49 cases, with complete

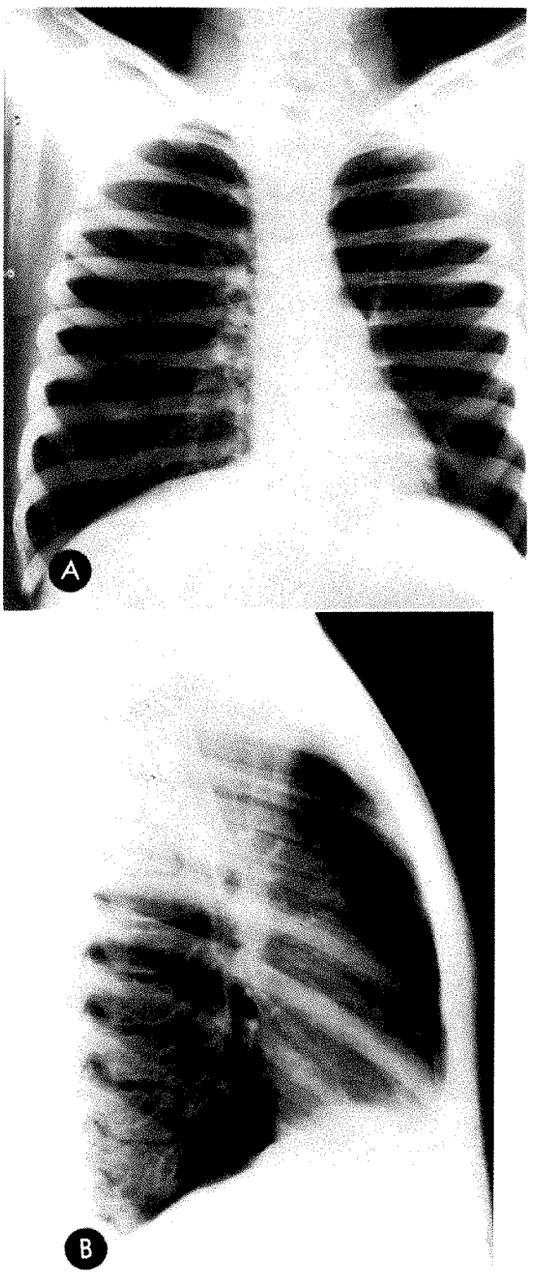


Fig. 11. (*A*) PA chest. Hyperinflation pattern; 10 year old male. Four month history of fever and cough. (*B*) Lateral, same patient.

excision of the roentgenographically abnormal region in 7 cases. (Two of these later developed disease involving other lobes.) In 3, the diagnosis was first made at autopsy; 7 other patients from this series came to autopsy for various reasons.

Bronchiolitis obliterans was manifest in several principal ways. Most commonly the respiratory bronchioles were filled with characteristic masses of organized exudate, histologically resembling nasal polyps (Fig. 12, *A* and *B*). Less frequently, peribronchial and mural infiltration by mononuclear cells and granulation tissue resulted in a constrictive bronchiolitis (Fig. 13). Least common in this series, and most difficult to detect on casual histologic examination, was total or subtotal obliteration of the bronchioles by scar (Fig. 14).

Other features varied according to the chronicity of the process, and whether it was diffuse or focal. The intrabronchiolar polyps were initially cellular, with lymphocytes and mononuclear cells predominating in a matrix of proteinaceous exudate rich in fibrin. Some also contained polymorphonuclear leukocytes. More "mature" polyps consisted of somewhat myxoid connective tissue containing fibroblasts. In some cases, central nests of plasma cells, lymphocytes and large mononuclear cells often replete with residual bodies were seen in many of the polyps. Many polyps were covered with respiratory epithelium, and some were converted into mounds of granulation tissue with a broad mural attachment encroaching on the small bronchioles (Fig. 15). In other regions the original lumen was converted into several channels, each lined by epithelium or obliterated completely by fusion of the polyp with the walls of the airway. The polypoid masses extended into alveolar ducts and alveoli to a variable extent, but were quite rare in small bronchi. Polypoid connective tissue proliferation was uncommon in cases with infiltrative or constrictive bronchiolitis.

The condition of the nearby airways varied from clear and overdistended (Fig. 14) to partly consolidated with severe interstitial thickening. The alveoli were filled with a variety of cellular constituents, but most notably with fat-filled phagocytes (Fig. 16). These foamy cells could be found in small numbers even in alveoli with relatively normal septa as well as in those alveoli with interstitial fibrosis and mono-

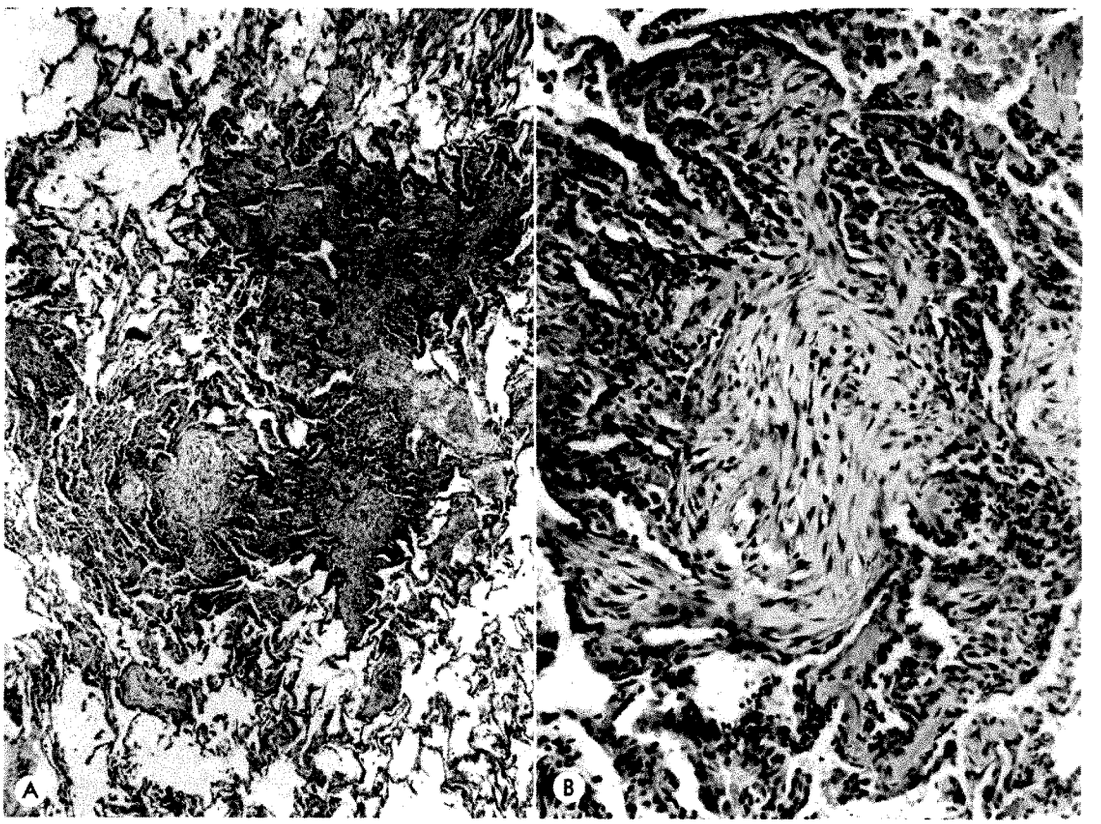


Fig. 12. (*A*) Low power photomicrograph. Intrabronchial and adjacent interstitial organization. Note normal alveoli in periphery of acinus (50×). (*B*) Detail, same field. Polypoid mass of organizing exudate filling bronchiole, the typical lesion (200×).

nuclear infiltration where they were more numerous, often aggregated into masses. In some foci the fat-filled mononuclear cells were found in large accumulations within the thickened walls of distal air spaces and occasionally within the intrabronchiolar polyps. In several cases large mononuclear cells released enough cholesterol for the characteristic acicular crystals to appear; in at least 1 case there was a marked giant cell reaction to the endogenous cholesterol. "Cholesterol" or "obstructive" or "endogenous lipid" pneumonia is often an important feature of bronchiolitis obliterans, sometimes so marked as to be confused with pneumonia due to exogenous lipid.

Interstitial infiltration with lymphocytes, plasma cells, and occasionally eosinophils was usually localized in the vicinity of the involved bronchioles (Fig. 12, *A* and *B*). In some cases interstitial infiltration appeared to be the predominant lesion, much more widely distributed than the bronchiolitis obliterans, suggesting that the latter was a complication of a diffuse interstitial pneumonia. Honeycombing, or end-stage scarring of the lung, was seen in 4 cases, although it was early and focal in 2. In many cases of severe interstitial pneumonitis of the usual type there is some bronchiolitis obliterans present, but these cases are not considered here. One case with interstitial pneumonia had many small granulomas, typical of hypersensitivity, in this case attributable to exposure to pigeons. Several other cases had occasional small granulomas; 1 had numerous sarcoid lesions causing bronchiolar obstruction.

One case in a child with focal total obliteration of bronchioles had diffuse pul-

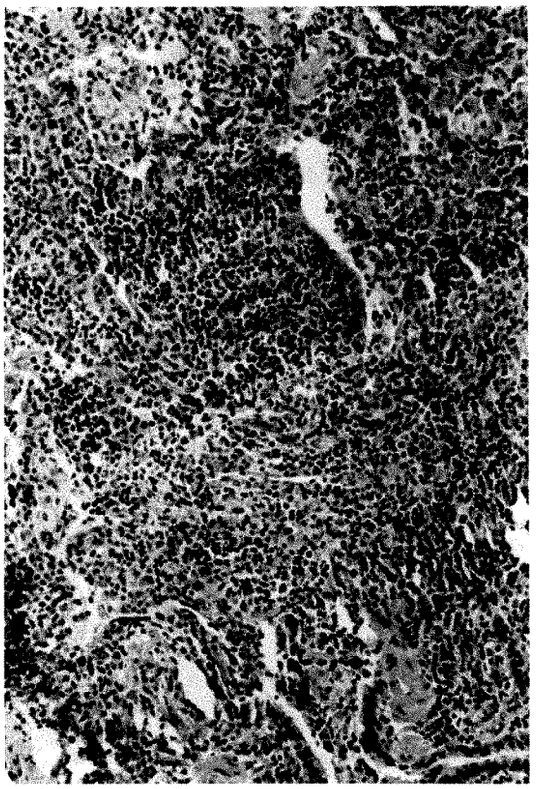


Fig. 13. Constrictive bronchiolitis. Note extensive peribronchial and mural infiltration by mononuclear cells and lymphocytes (200×).

monary hyperinflation and an "emphysematous" appearance. This may be considered bilateral "radiolucent lung" syndrome[15,28] in a child (Fig. 14). These findings were consistent with the bronchiolar obstruction described in several cases studied pathologically.[25] Another case with similar histologic findings did not show overinflation of the lungs, but the roentgenograms also under-represented the severity of parenchymal damage as suggested by severe functional impairment. Some small airways could be detected only as scars adjacent to small pulmonary arteries (Fig. 14); in others there was "recanalization" (Fig. 17) with one or more epithelial-lined channels, such as with organization in arterial thrombosis. Another case with such obliterative changes had an infiltrative bronchiolitis, but typical polyps and some evidence of bronchiolectasis in various regions.

Roentgenologic-Pathologic Correlation

There is no direct correspondence between roentgenographic patterns and histologic findings to be found in this material. The advantage of surgical biopsy material for these studies, in being free of the usual terminal or aspiration pneumonia and the damage from respirator treatment with oxygen, is balanced by the disadvantage of restricted sampling of the lung. While a small biopsy may reveal the pathogenesis of the pulmonary disease, it often does not explain the distribution of findings seen roentgenologically. A further sampling problem is the absence of small and large bronchi in most biopsies. Although the discussion here centers on bronchiolitis obliterans, the extent of disease further

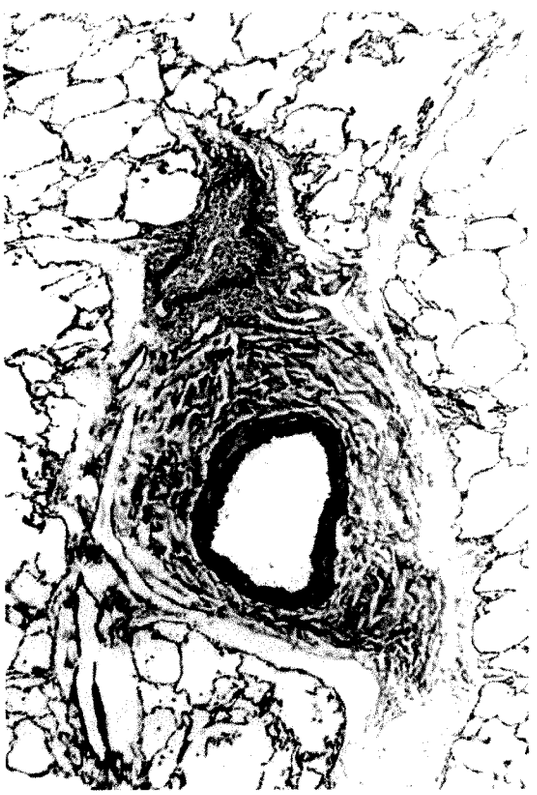


Fig. 14. Total focal bronchiolar obliteration (elastic tissue stain). The shrunken bronchiole, adjacent to a patent pulmonary arteriole with adventitial fibrosis, is outlined by its elastica. Note surrounding hyperinflated parenchyma, evidence of collateral ventilation (80×).

proximal would clearly affect the roentgenologic distribution of findings. Nodules demonstrable roentgenologically in this disease were usually 2–3 mm. in size (micronodular or lineonodular) or just under 1 cm. in size (discrete nodular). Nodules of appropriate size were not always demonstrated in the histologic material from these cases, although round infiltrates were seen on many slides from the entire series. It must be conjectured that micronodular shadows represent the focal interstitial infiltration and intra-alveolar accumulation of exudate including the fat-filled phagocytes around an obstructed respiratory bronchiole, but not the entire acinus represented by the discrete nodular shadow. The lineonodular patterns were almost all associated with considerable interstitial pneumonia or fibrosis, although half the micronodular cases were as well.



Fig. 15. Organized polypoid mass covered by respiratory epithelium encroaching on the lumen of a bronchiole. Healing stage, although lymphocytic infiltrate persists (200×).



Fig. 16. Abundant fat-filled phagocytes, many incorporated into interstitium by overgrowth of epithelium (200×).

The large number of cases with atelectasis or segmental and lobar opacification suggests that many small and subsegmental bronchi were also filled with organized exudate, although this could not be documented in this material. Few of these cases had significant interstitial fibrosis aside from focal changes around obstructed bronchioles. In a search for means of identifying cases with a hypersensitivity component, histologic findings of abundant plasma cells or acid mucopolysaccharides were compared with the roentgenologic pattern or clinical syndrome. There was no correlation between these findings and either the roentgenographic pattern or over-all course. The finding of small granulomas, sarcoid-like, also failed to pinpoint any particular syndrome or roentgenologic pattern in the majority of the 8 cases. Finally, the focal scarring of airways with

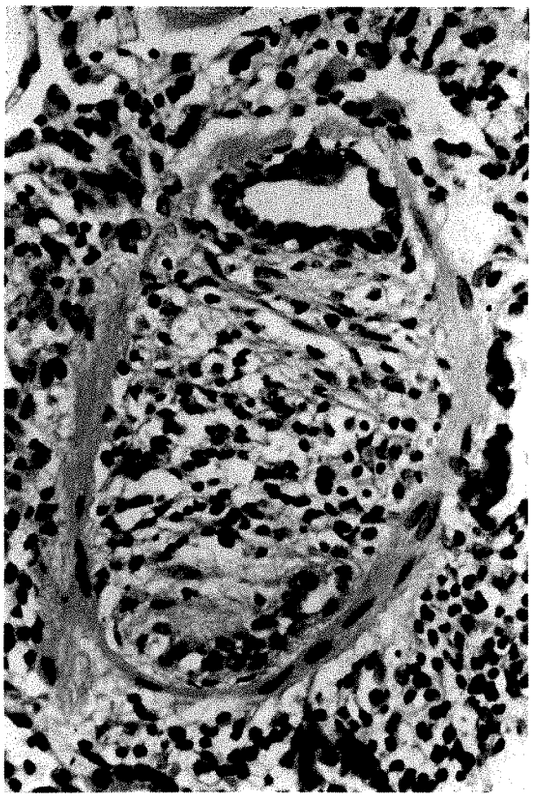


FIG. 17. Partial recanalization of occluded bronchiole. Note original size indicated by persistent smooth muscle outline (500×).

adjacent alveolar overexpansion matched the roentgenographic appearance of pulmonary hyperinflation in 1 case, but correlated poorly in the other case of roentgenographic hyperinflation, or the other cases with histologic evidence of focal air-trapping.

CLINICAL COURSE AND THERAPY

In patients who developed bronchiolitis obliterans, the etiology could be classified into one of 4 major categories: (1) post-pneumonic; (2) chronic or recurrent respiratory disease; (3) toxic inhalation (including aspiration); and (4) unknown etiology.

In our series, there were 18 patients in the post-pneumonic group. These individuals were generally in good health until sudden onset of a lobar or subsegmental pneumonia. When the pneumonia failed to clear adequately with treatment, lung biopsy was obtained and bronchiolitis obliterans was recognized as a component of the disease. In these cases, bronchiolitis obliterans was obviously secondary to bacterial or viral infection. There was some overlap with the chronic respiratory disease category.

The second group included 11 patients with lifelong histories of chronic bronchitis, asthma, or recurrent respiratory tract infections. As previously noted, 3 of these patients were also classified in the post-pneumonic group.

In the third group there were 8 cases of toxic inhalation, only 1 being acute. This patient, exposed to nitric oxide fumes, had the typical biphasic course consisting of rapid onset of pulmonary edema clearing spontaneously, followed by a lag period of 1–2 weeks and succeeded by an even more intense and longer-lasting episode of diffuse alveolar opacities and respiratory distress. This pattern has been fully described elsewhere.[18,27] Four of these patients had co-existent major disease.

The fourth group included many patients, who could not be classified in any definite category; the nature and etiology of the disease were unclear from the start. Clinical and laboratory observation were of little help in elucidating the cause of the patients' symptoms. These patients were treated largely on an empirical basis.

Eleven deaths occurred among the 52 patients, 7 in individuals with no known etiology for their disease. Five of these patients showed nodular densities on their roentgenograms, and 3 demonstrated a segmental or lobar pattern.

In addition to symptomatic treatment and respiratory support, where necessary, many patients were treated with a variety of antibiotics, steroids or combinations of the 2. We have specific information relating to such treatment in 40 patients (Table VII). Of 17 patients treated with steroids alone, 15 showed partial or complete (6) improvement. Of 5 treated with antibiotics alone, 3 showed improvement (1 complete). Of 18 patients treated with a combination

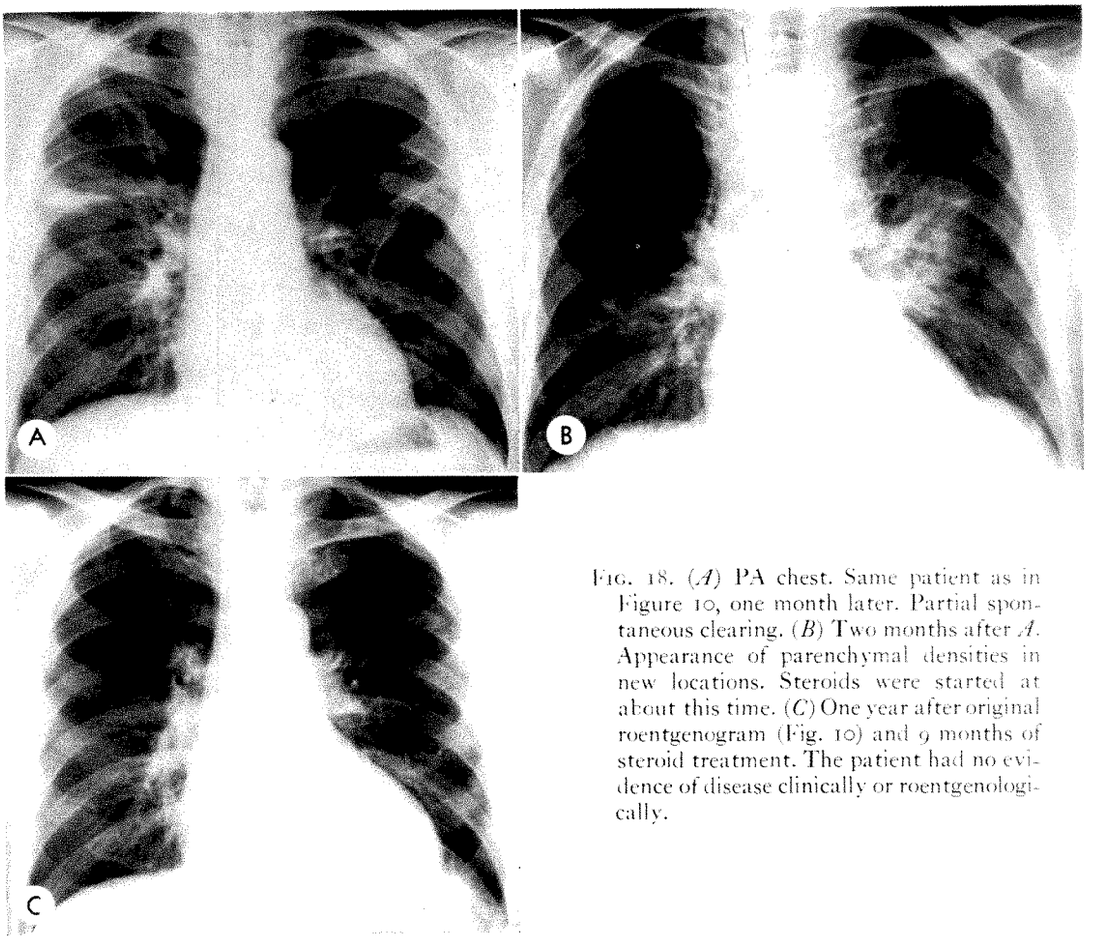


Fig. 18. (*A*) PA chest. Same patient as in Figure 10, one month later. Partial spontaneous clearing. (*B*) Two months after *A*. Appearance of parenchymal densities in new locations. Steroids were started at about this time. (*C*) One year after original roentgenogram (Fig. 10) and 9 months of steroid treatment. The patient had no evidence of disease clinically or roentgenologically.

of antibiotics and steroids, 10 improved (5 complete).

Of 11 patients with post-pneumonic disease, 3 showed improvement with steroids alone, and 1 improved with antibiotics alone. When combination therapy was employed, 3 patients improved, 4 demonstrated no change. Seven underwent complete excision of the affected area (5 with no other treatment), but of these only 1 recovered completely. Two of these patients died shortly afterwards, 2 showed continuing disease in other sites. In 2 more, there was no follow-up.

Of the 11 chronic pulmonary disease patients, 3 improved with steroids alone and 1 with antibiotics alone. Of 6 patients treated with the combination, 5 improved. In another patient the lesion was resected with disease developing later in another lobe.

In the toxic inhalation category no patients were treated with antibiotics alone. Of the total of 8 patients, 2 were given steroids alone (1 improved) and 5 were given the combination of medications (3 improved). One patient had resection of his lesion; however, he died shortly afterwards.

Of 21 patients with bronchiolitis obliterans of unknown etiology, 3 patients were given combination treatment—1 improved and 2 died. Four patients were given antibiotics alone and 1 showed complete improvement. Two died, 1 after temporary improvement. Nine patients were given steroids alone and 7 showed lasting improvement (Fig. 18, *A–C*). One showed

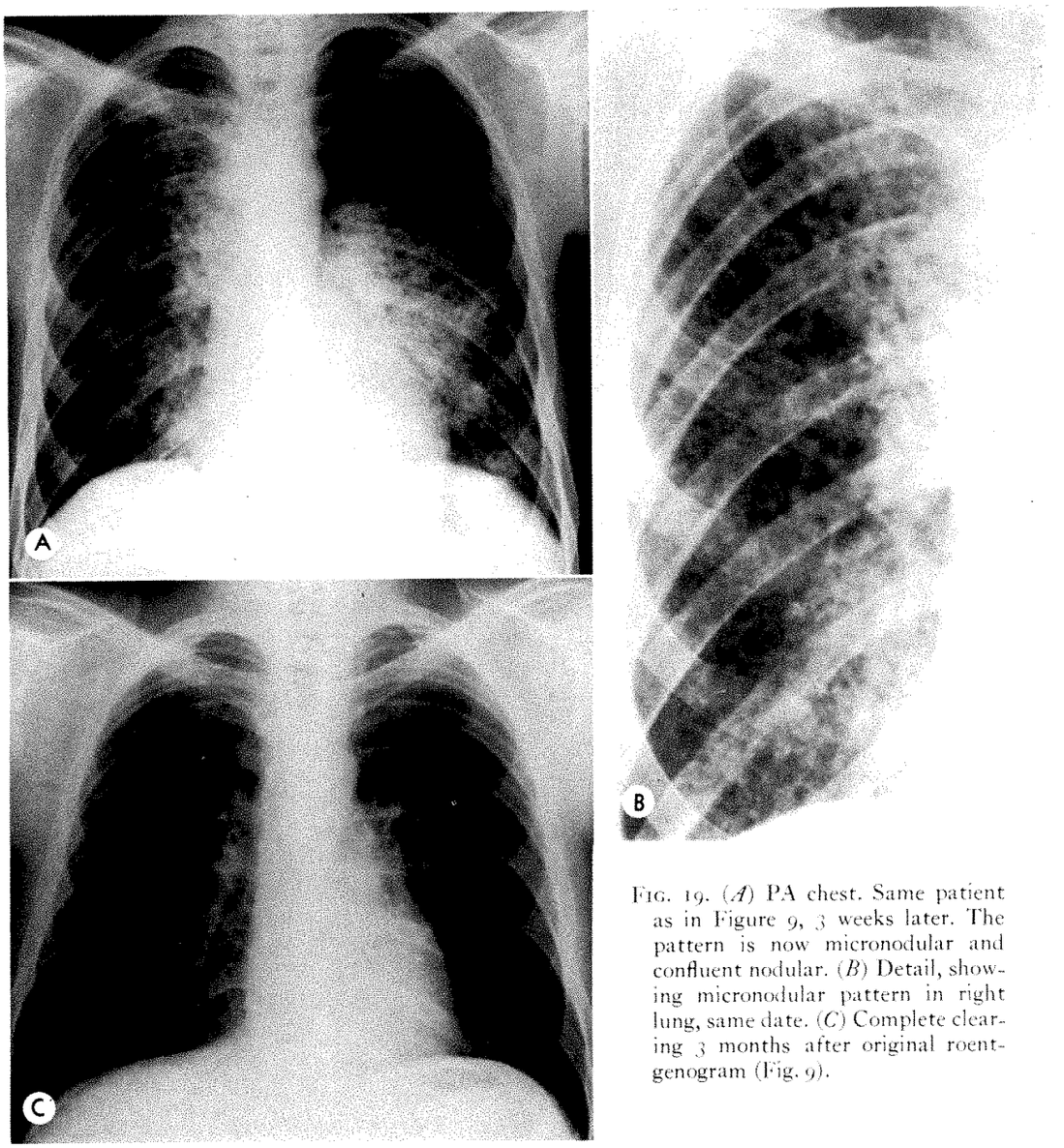


Fig. 19. (*A*) PA chest. Same patient as in Figure 9, 3 weeks later. The pattern is now micronodular and confluent nodular. (*B*) Detail, showing micronodular pattern in right lung, same date. (*C*) Complete clearing 3 months after original roentgenogram (Fig. 9).

temporary improvement, but later died. Of 4 patients receiving no specific treatment, 2 improved.

Thus it is clear that steroids may be of considerable benefit, even in the absence of a significant component of proven hypersensitivity.

Correlations between roentgenographic patterns and clinical course

Some interesting relationships were noted between the roentgenographic pattern and the clinical course (Table VIII). Cases with a *micronodular* roentgenographic pattern fell into 2 classes clinically. Three of the 5 patients had symptoms and roentgenologic findings which cleared readily on steroids or antibiotics, without evidence of residual disease. Two patients appeared much more severely affected, and also had more prominent pulmonary infiltration roentgenologically. One of these died, and had evidence of *Klebsiella* infection at postmortem ex-

Table VII

RESPONSE TO THERAPY

Pathogenesis	Steroids	Antibiotics	Combination	Surgery	No Specific Treatment
Post-pneumonic (18 patients)	PI (2) (1 with later resection) CI (1)	PI (1) (also in chronic infection category)	PI (1) CI (2) (1 complete hiatal hernia repair*) NC (4) (1 with later resection and death)	Resected: 5 (1 death, 1 CI, 2 CD, 1 no FU)	1 CD, 1 no FU
Chronic pulmonary infection (11 patients)	PI (2) CI (1)	PI (1) (also in post-pneumonic category)	PI (3) CI (2) (1 complete hiatal hernia repair*) NC (1) (also in post-pneumonic category)	Resected: 1 CD (also in post-pneumonic category)	
Toxic inhalation (including aspiration; 8 patients)	PI (1) NC (1)		PI (1) CI (2) (1 complete hiatal hernia repair*) Death (2)	Resected: 1 (death) (also in post-pneumonic category)	
Unknown etiology (21 patients)	PI (4) (1 improved temporarily, death later) CI (4) (1 later unrelated death) NC (1)	PI (1) (improved temporarily, death later) CI (1) NC (1) Death (1)	CI (1) Death (2)		4 (2 CI, 1 death, 1 no FU)

PI = partial or temporary improvement; CI = complete improvement; CD = continuing disease; FU = follow-up; NC = no change; * = same patient.

amination; the other had pre-existing uremia, but nevertheless recovered after a stormy course (Fig. 19, *A–C*).

The 5 patients with *lineonodular* opacities were consistent in having a longer history of active disease. Improvement was obtained by treatment with steroids and antibiotics together in most cases, but in 4 with follow-up there was residual clinical or roentgenologic abnormality.

The effects of disease were more severe in patients with *discrete nodular* or *confluent nodular* densities on chest roentgenograms. Only 2 of the 9 patients (2 fell into both categories) in these categories recovered completely; 5 died, and 1 is chronically ill at this time. One patient had no follow-up reported.

In the groups with *basilar opacities* and *multiple irregular* or *diffuse alveolar opacities*, there were few cases of complete recovery among those with adequate follow-up (6/15). Nearly all those with substantial improvement had been treated with steroids (4/6). In the group with *lobar* or *segmental* disease, 7 had removal of diseased lung by surgery with 2 postoperative deaths and 2 others with continuing or recurrent lung involvement (Fig. 20). One showed complete improvement. About half of those treated primarily by medical means either died or had residual lung disease; only 1 patient had apparently com-

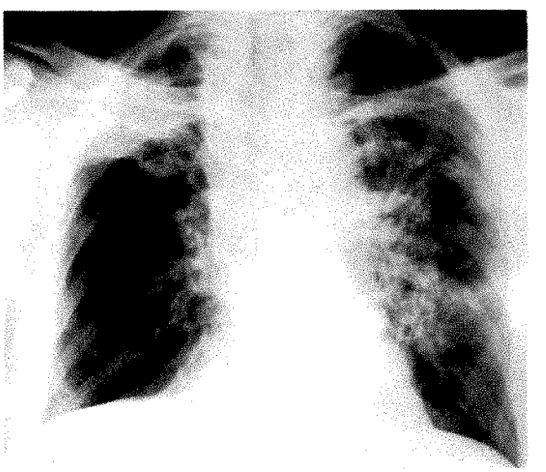


Fig. 20. PA chest. Same patient as in Figure 8, 5 months later. Involvement of additional parts of the lungs in patient with recurrent aspiration. The chest roentgenogram cleared completely on a combination of antibiotics and steroids, following a hiatal hernia repair.

TABLE VIII

RELATIONSHIP BETWEEN ROENTGENOGRAPHIC PATTERN AND CLINICAL COURSE

	Complete Improvement	Continuing Disease and/or Residua	Death	No Follow-up
Micronodular	4 (1 overlap with diffuse opacities)	0	1 (1 overlap with confluent nodular)	0
Discrete nodular	0	1 (1 overlap with lobar)	3 (2 overlap with confluent nodular)	1 (overlap with basilar opacities)
Confluent nodular	2	0	4 (2 overlap with discrete nodular; 1 overlap with micronodular)	0
Lineonodular	0	4 (1 overlap with multiple opacities; 1 overlap with lobar)	0	1
Bibasilar	3	4	1	2 (1 overlap with discrete nodular; 1 overlap with lobar)
Lobar or segmental	2 (1 overlap with multiple opacities)	9 (1 overlap with discrete nodular; 1 overlap with hyperinflation; 1 overlap with lineonodular)	3	6 (1 overlap with bibasilar opacities)
Diffuse (edema-like)	1 (overlap with micronodular)	0	1	0
Multiple opacities	2 (1 overlap with lobar)	2 (1 overlap with lineonodular)	1	3
Hyperinflation	0	2 (1 overlap with lobar)	0	0
Total	12 (2 overlap)	18 (4 overlap)	11 (3 overlap)	11 (2 overlap)

plete recovery, without lung resection, and this was after hiatal hernia repair in addition to medical treatment. Follow-up was insufficient in 6 others. These figures suggest that even apparently localized disease was not readily treated with success, and that a significant number of patients develop new manifestations of pulmonary disease eventually (Fig. 10, *A* and *B*; and 18, *A–C*).

Attempts to correlate the roentgenographic patterns with the pathologic findings failed to yield significant results. This may be because the lung specimens represented many different stages of organization, as well as somewhat varied manifestations of bronchiolar obstruction, and only few showed obviously irreversible bronchial scarring or parenchymal honeycombing. It was also difficult to tell if a lung biopsy was representative of the predominant pattern of lung involvement. Since etiology was obscure in the great majority of cases, there was no convenient bridge between pathologic and clinical manifestations or roentgenographic findings.

SUMMARY

Bronchiolitis obliterans is a pathologically defined syndrome of bronchiolar ob-

struction by organizing exudate, often associated with cholesterol and interstitial pneumonia.

Among 52 cases with roentgenograms available for review, few were associated with specific etiologic factors. Several patients had co-existent systemic disease.

Although occasionally a localized process amenable to surgery, bronchiolitis obliterans was usually diffuse, causing pulmonary insufficiency and death in some, but resolving in others.

Administration of steroids was usually associated with clinical improvement.

Roentgenologic patterns included: nodular densities (micronodular, discrete, confluent and lineonodular); alveolar opacities (diffuse, multiple irregular or bibasilar); and hyperinflation.

Early recognition of this syndrome may permit treatment before irreversible changes develop.

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CAVITATING PULMONARY METASTATIC DISEASE IN CHILDREN*

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CAVITATING pulmonary metastatic neoplasms in children are rare. The roentgenographic and morphologic evolution of 3 different primary tumors that metastasized to the lungs are described and the literature is reviewed.

REPORT OF CASES

CASE I. A 17 year old girl was admitted to the hospital because of post-traumatic pain in the distal left thigh. Osteogenic sarcoma was diagnosed roentgenographically and was confirmed by open biopsy. The patient received a full course of radiation therapy after which the left lower extremity was amputated at the midthigh. Eighteen months later, metastatic pulmonary nodules had developed (Fig. 1*A*). Pleuritic chest pain and a right pleural effusion were documented.

During the next 2 years, the metastatic pulmonary nodules increased in size and number despite intensive chemotherapy (actinomycin, vincristine, and cytoxan), irradiation, and palliative surgical excision (Fig. 1, *B–D*).

CASE II. A 10 month old boy had lethargy, anorexia, and weight loss. A large right-sided abdominal mass was palpated. Urography revealed a Wilms' tumor and a surgical resection was performed. The infant received actinomycin D and radiation therapy. Eight months later pulmonary metastases had developed. The cavitated pulmonary tumor nodule was excised (Fig. 2, *A* and *B*). Dactinomycin was administered and the right lung was irradiated. No disease has been evident in the past 2 years.

CASE III. A hematoma developed in the left hip of a 6 year old girl subsequent to a fall. Five months later the hematoma recurred and biopsy revealed only cystic hematoma. The patient was anemic and had generalized lymphadenopathy, hepatosplenomegaly, and an increased sedimentation rate.

Six months later, the arteriographic appearance was normal, but biopsy of the capsule of the lesion showed connective tissue reaction with masses of spindle cells, and the findings were considered non-neoplastic. Biopsy of the inguinal lymph nodes, however, revealed a well differentiated metastatic angiosarcoma.

Four years after the symptoms had begun, an angiosarcoma of the left buttock region was excised. The tumor extended to the margin of the excised tissue. The area of excision was irradiated postoperatively. Bilateral pulmonary metastatic nodules developed with cavitation of those in the left upper lobe (Fig. 3). Thorough investigations of non-metastatic causes of pulmonary cavitation were repeatedly normal.

DISCUSSION

Incidence. Cavitating pulmonary metastases are most uncommon lesions; the 79 cases reported in the literature included only 1 child.[7] In this child, with histologically proved Wilms' tumor, cavitation of pulmonary metastatic nodules developed after roentgen therapy. D'Angio[5] has kindly shown us roentgenograms of another child with metastatic Wilms' tumor in whom a large cavitary pulmonary lesion developed. D'Angio and Iannaccone[6] reported spontaneous pneumothorax in children with pulmonary metastasis and suggested that cavitation of some metastatic nodules and their rupture in the pleural space may be the cause of this type of pneumothorax.

In 1961, Dodd and Boyle,[8] in a review of 6,729 consecutive adult chest roentgenograms, found 176 primary lung tumors and 398 metastatic tumors. Cavitation was roentgenographically detectable in 36 (9 per cent) of primary tumors and in 16 (4 per cent) of metastatic tumors. Excluded were cases in which cavitation was detected

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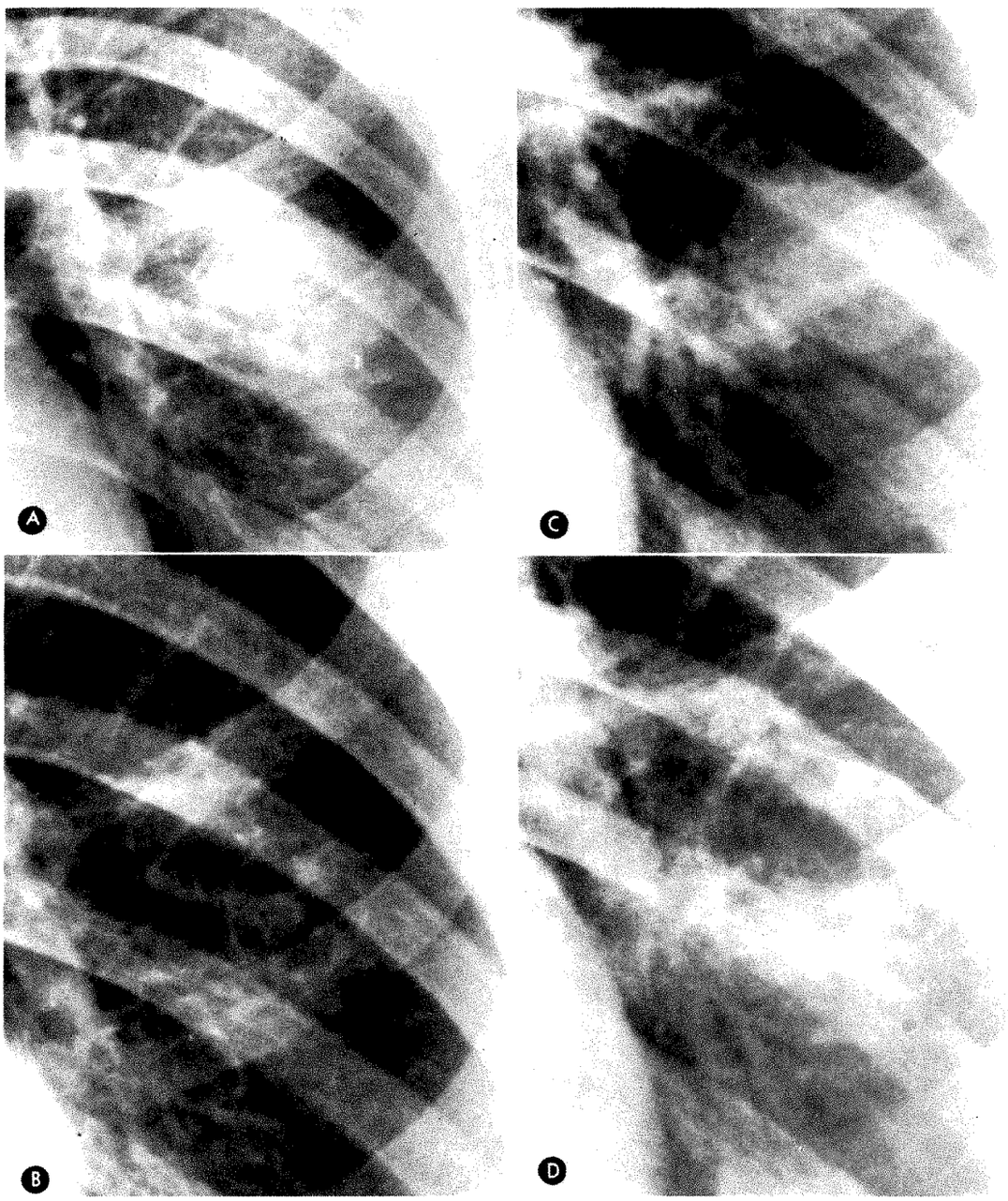


FIG. 1. Case 1. Metastatic osteogenic sarcoma. (*A*) Initially, a spherical, solid metastatic nodule of 3 cm. in diameter was present in the left mid-lung. Multiple other metastatic lesions also were present. (*B*) Three months later, after roentgen therapy and chemotherapy, the previously described lesion decreased to 2 cm. in diameter and became a thin-walled, air-filled cavity. At its lateral basal aspect, a focal thickening of the walls perhaps represented residual tumor. (*C*) Two months later, concomitant with progressive metastatic disease in the right lung, the left mid-lung nodule became homogeneously opacified and increased in size to 3.1 cm. in diameter. (*D*) One month later, this lesion was a thin-walled cavity 3.6 cm. in diameter.

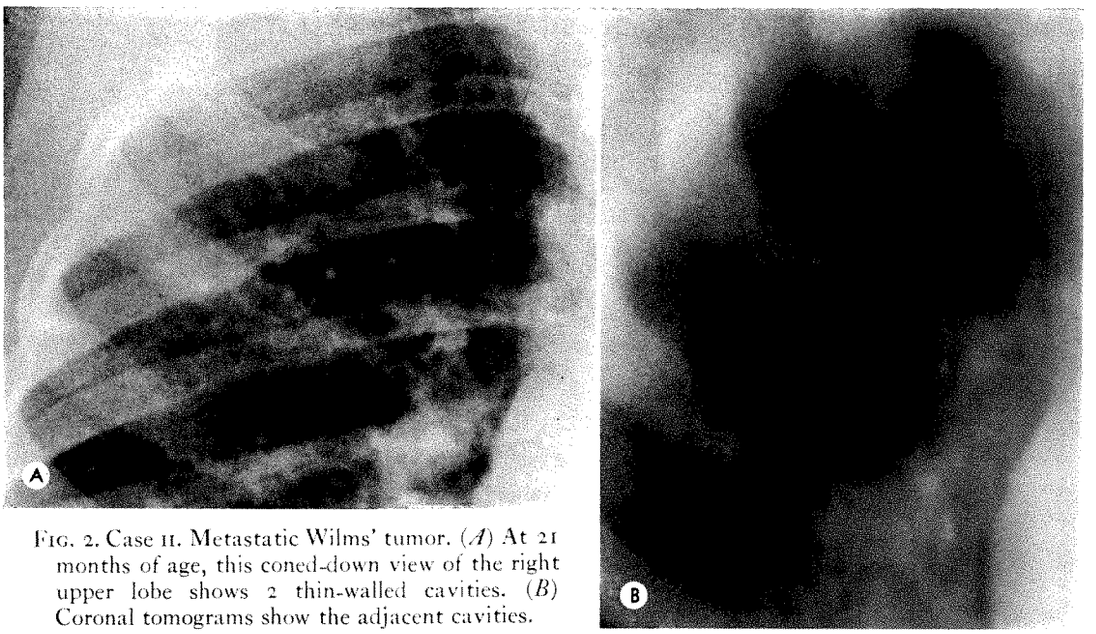


FIG. 2. Case II. Metastatic Wilms' tumor. (*A*) At 21 months of age, this coned-down view of the right upper lobe shows 2 thin-walled cavities. (*B*) Coronal tomograms show the adjacent cavities.

after chemotherapy or local roentgen therapy and those with a solitary metastatic neoplasm.

Histologic features. In the 16 cases of adult cavitary metastatic tumors reported by Dodd and Boyle,[8] 69 per cent were of squamous cell origin. Table 1 shows that of all reported cases of pulmonary cavitary metastases with histologic documentation, 45 per cent (29/64) arose from metastatic squamous cell carcinoma and 33 per cent (21/64) from metastatic adenocarcinoma. In 15 additional reported cases, cavitary pulmonary metastasis was not documented histologically.

Roentgenographic aspects. The thickness of walls of cavitating pulmonary metastatic lesions may vary from 1 to 15 mm.[17] The size of the cavity also varies considerably, the diameters ranging from 5 to 75 mm. Frequently, the walls of small cavities may be thick and those of larger cavities thin. The presence of several excavating nodules of different size is frequently observed in pulmonary metastasis[12] which cavitate. Cavitation may take place in only a few nodules, although metastatic growths may be numerous. Sometimes the cavities are multilocular and resemble cystic disease. The upper lobe is most frequently involved.

Pathogenesis. Many explanations may be considered for the cavitation.

(a) Cavitation may result from necrosis

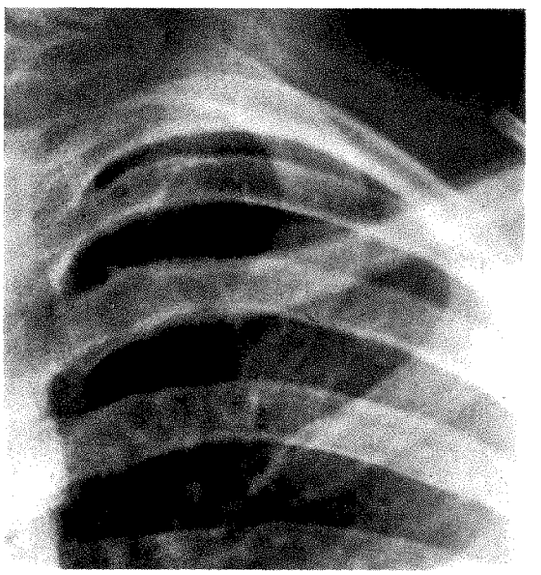


FIG. 3. Case III. Metastatic angiosarcoma. In the left apex, a spherical, thin-walled, air-filled cavity of 13 mm. in diameter is seen. In addition, several other solid metastatic lesions were identified elsewhere.

TABLE I

REVIEW OF PREVIOUSLY REPORTED CASES OF CAVITATING PULMONARY METASTASIS ACCORDING TO HISTOLOGIC TYPE AND SITE OF PRIMARY TUMOR

Histologic Type	Site of Primary Tumor	Authors	Number of Cases Reported	Total Cases
Squamous cell carcinoma	Pharyngolarynx	Dodd and Boyle[8]	4	
		Bristowe[2]	1	
		LeMay and Piro[17]	2	7
	Female genitalia	Dodd and Boyle[8]	5	
		Don and Gray[10]	4	
		Wigh and Gilmore[29]	1	
		Lowen[19]	1	
		Seaman and Arneson[25]	1	12
	Lung	Meyers and Sala[21]	1	
		Wellens[28]	1	
		Deck and Sherman[7]	1	3
	Bladder	Minor[22]	1	
		Deck and Sherman[7]	1	2
	Penis	Wellens[28]	1	
	Tongue	Gellman and Jelliffe[13]	1	
	Unknown	Minor[22]	3	5
				29 (45 per cent)
Adenocarcinoma	Colon, rectum	LeMay and Piro[17]	5	
		Dodd and Boyle[8]	3	
		Katzev and Bass[15]	1	
		Curran and MacCarthy[4]	1	
		Lowen[19]	1	11
	Kidney	Grossman *et al.*[14]	1	1
	Breast	Dodd and Boyle[8]	2	2
	Pancreas	Salzman *et al.*[24]	1	
		Lowen[19]	1	2
	Breast and pancreas	Laforet and Laforet[16]	5	5
				21 (33 per cent)
Transitional cell carcinoma	Bladder	Dodd and Boyle[8]	1	
		LeMay and Piro[17]	1	
		Weintraub[27]	1	3
Undifferentiated carcinoma	Unknown	LeMay and Piro[17]	1	1
Seminoma	Testes	Salzman *et al.*[24]	1	1
Teratocarcinoma	Mediastinum	Laforet and Laforet[16]	1	1
Sarcoma	Unknown	Farrell[11]	1	
		Baldry[1]	1	2

Table I—*Continued*

Histologic Type	Site of Primary Tumor	Authors	Number of Cases Reported	Total Cases
Osteogenic sarcoma	Bone	Dolgoff and Hansen[9]	1	
		Rigler[23]	1	
		Lichtenstein[18]	1	
		Deck and Sherman[7]	1	
		Crow and Brogdon[3]	1	5
Wilms' tumor	Kidney	Deck ahd Sherman[7]	1	1
				14 (22 per cent)
Total				64

of the central portion of the tumor, possibly because of inadequate circulation with subsequent ulceration into a bronchus, and, finally, ejection of the necrotic material.[30] This possibility does not explain the very small tumors with thin walls. Furthermore, occasionally, at necropsy, no central necrosis is found.

(b) Occasionally cavitation may be related to a characteristic property of the squamous epithelium.[8] When a membranous squamous epithelium is exposed to the atmosphere, its surfaces dehydrate and form a keratinized layer that is replaced by another layer of squamous epithelium. Possibly, in pulmonary metastasis, the communication with a small bronchus or an alveolar duct is established early, the keratinized layers are shed, and a cavity results. This postulated mechanism may be operational in small tumors with thick walls.

(c) For the tumors with thin walls, the mechanism of cavitation is uncertain, but does not seem to be related to infection. Perhaps the tumor cells cause a ball-valve type of bronchial obstruction with growth of the tumor in a distended air space.[26]

(d) Another mechanism possibly present in some metastatic adenocarcinomas is the tendency to cystic degeneration.[8]

(e) Occasionally a pseudocavitation may be seen in which the central necrosis develops with liquefaction, but no evacuation, of the necrotic material.[14] Thus, roentgenographically, a ring shadow is produced when the density between the central and peripheral portions of the tumor is different.[20]

In the first 2 patients, the pulmonary lesions cavitated during the course of chemotherapy and radiation therapy. Undoubtedly the centers of these tumors underwent necrosis, and because they communicated with the bronchus, the necrotic tumor tissue was coughed out. With subsequent regrowth of the tumor, however, these lesions resolidified. Following excision they were found to be completely filled with viable tumor cells.

The third patient (Case III) has a unique blood vessel tumor that forms large cavernous spaces in the course of its growth and does not evolve in the usual mechanism of forming a progressively enlarging ball of cells. This tumor may appear solid intermittently because it contains blood in the lumen of its spaces, but because of communication with the bronchus the blood is coughed out.

The differential diagnoses of cavitating pulmonary metastasis in children include abscess or pneumatocele (especially that caused by staphylococcus), communicating cystic lesions (such as bronchogenic cyst), tuberculosis, aspergillosis, coccidioidomycosis, varicella, and xanthomatosis. Since many of these conditions are possible complications in malignant tumors, they should be excluded on clinical and laboratory

bases. In some instances, only surgical resection and histologic examination of the specimen will reveal the nature of the cavitating pulmonary metastases.

Cavitation of the metastatic nodules does not influence the course of the disease or the prognosis any more than do other metastatic growths. Nearly all patients with pulmonary metastasis died, whether or not the tumor nodules were cavitated.

SUMMARY

Three cases of cavitating pulmonary metastasis in children are reported.

A review of the literature produced only 79 published cases; only 1 of the patients previously described was a child.[7]

The histolgic appearance of the primary tumors, the roentgen aspects, and the pathogenesis are reviewed.

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ROENTGENOLOGIC APPEARANCE OF THE CHEST FOLLOWING RADICAL NECK DISSECTION*

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CERVICAL metastases are frequently treated surgically by radical neck dissection. Ewing and Martin[1] discussed the disability and resultant deformity, and Gorman *et al.*[2] attributed the characteristic deformity in the region of the sternoclavicular joint to clavicular subluxation and rotation.

Following radical neck dissection there is a characteristic chest roentgenographic appearance not previously described in the literature or in standard text-books.

This paper describes those findings which should lead the observer to the roentgenologic diagnosis of a previous radical neck dissection in the absence of historical information on the consultation requests.

SURGICAL CHANGES

Despite minor variations popular among a few surgeons, a standard neck dissection can be accurately described.[3] The area of dissection is bounded superiorly by the body of the mandible, the lower third of the parotid gland, the roof of the jugular fossa, and the mastoid process. The posterior boundary is the anterior margin of the trapezius muscle, while the inferior border is the clavicle. The anterior border includes the submental space above the hyoid, and below the hyoid it descends in the midline to the suprasternal notch. Dissection of, but not including, the scalene, erector spinae, levator scapulae, and myohyoid muscles defines the deep boundary. This dissection removes the sternocleidomastoid muscle, the omohyoid muscle and often the posterior belly of the digastric muscle and the stylohyoid muscle. Other structures removed include the submandibular gland and the lower third of the parotid gland, the spinal accessory nerve, the internal jugular vein and all major cervical lymphatics to the borders of the dissection. When tumor cannot be cleared from the external carotid artery it too may be sacrificed if removal appears to leave the area tumor free.

Extensions of the standard radical dissection most often include dissection of the platysma from the skin, mandibular resection *en bloc* when lymph nodes are attached, and inferior extension into mediastinal area for retroclavicular and retrosternal lymph nodes.

Occasionally a limited neck dissection is described which preserves the internal jugular vein and spinal accessory nerve but, since it so frequently leaves residual tumor in the lymphatics, it is judged less effective.

The 5 roentgenologic signs of radical neck dissection described below will allow the roentgenologist to appreciate that the patient has had radical neck surgery when historical information is lacking.

ROENTGENOLOGIC CHANGES

Standard radical neck dissection in 30 consecutive patients has resulted in 5 roentgenologic findings which occur with varying frequency (Table 1).

The hyperlucent supraclavicular fossa occurs because of the absence of the supraclavicular muscle mass, chiefly the sternocleidomastoid muscle. The frequency with which a striking asymmetry of supraclavicular density occurs approaches 93 per cent. The accuracy of diagnosis based on this finding alone however is low, for

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TABLE I

SUMMARY OF ROENTGENOLOGIC FINDINGS

Finding	Frequency
Hyperlucent supraclavicular fossa	28/30
Absent sternocleidomastoid muscle	23/30
Medial continuation of ipsilateral companion shadow	19/30
Drooping shoulder	20/30
Supraclavicular subluxation	8/30

most chest roentgenograms reveal some supraclavicular asymmetry in normal patients. In the immediate postoperative period in particular, this finding is usually absent due to edema. Absence of the sternocleidomastoid muscle is seen in about 77 per cent of patients having radical neck dissection and this diagnosis is confirmed when seen in association with a companion shadow atop the clavicle which extends to the sternum without ending in the characteristic upswing along the sternocleidomastoid muscle (Fig. 1). This asymmetric companion shadow is present in about 63 per cent of radical neck dissections. The interruption of the spinal accessory nerve together with the muscular resections will result in a drooping pectoral girdle with low lying scapula in about 69 per cent of patients. This defect appears to precede the sternoclavicular subluxations described by Gorman *et al.*,[2] as a late finding occurring only 33 per cent of the time following radical neck dissection (Fig. 2). Any combination of the above findings should lead to a firm diagnosis of previous radical neck dissection. We have discovered no false positive combinations of signs. A particularly challenging situation occurs when a patient has had bilateral neck dissections. A high index of suspicion together with absence of sternocleidomastoid muscles and medial extensions of both companion shadows may be the chief clues in such instances, for the usual asymmetry will be lacking (Fig. 3).

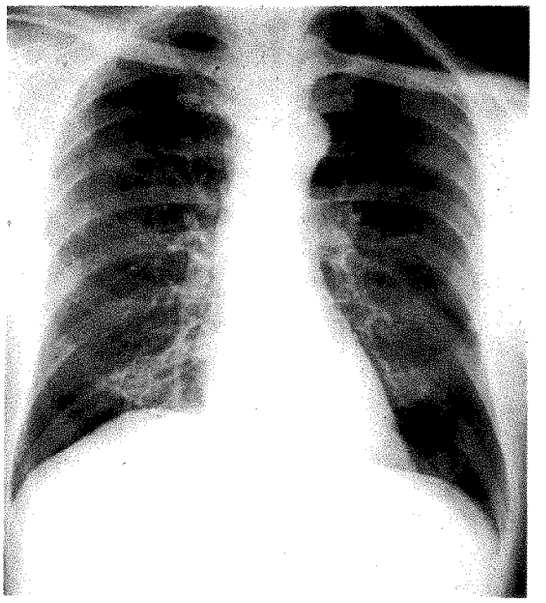


FIG. 2. All 5 findings are present in this patient. Note the sternoclavicular asymmetry with both rotation and upward migration of the medial left clavicle.

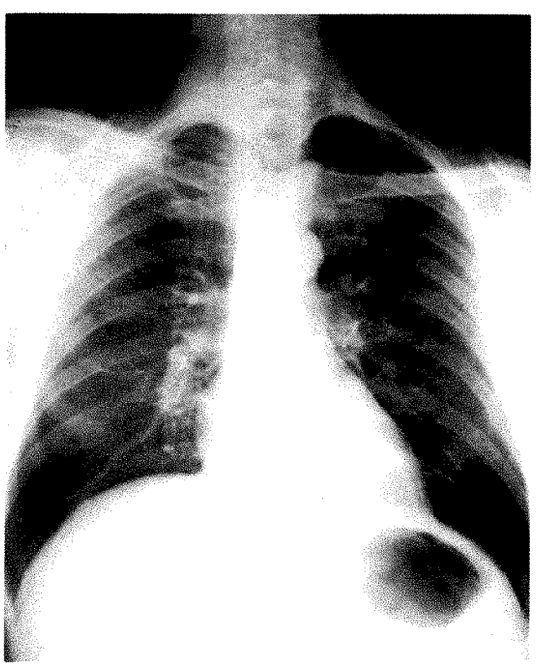


FIG. 1. This patient clearly shows the asymmetric supraclavicular fossae, companion shadows, and sternocleidomastoid muscles. The shoulder on the ipsilateral side has rotated lower because the spinal accessory nerve is cut, but as yet there is no sternoclavicular subluxation.

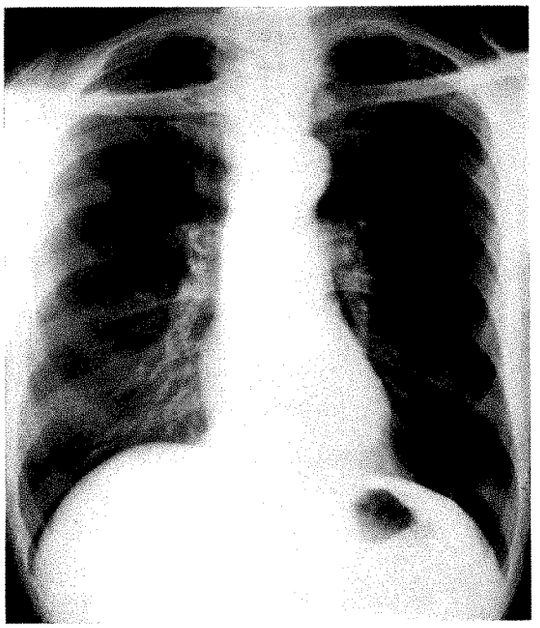


FIG. 3. The bilateral neck dissection patient may be particularly difficult to diagnose because of the lack of any asymmetry. In this patient the hyperlucency of the supraclavicular fossae, the absence of sternocleidomastoid muscles, and the medial continuation of companion shadows suggest the diagnosis which history confirmed.

SUMMARY

While a radical neck dissection poses no clinical diagnostic problem, this diagnosis is frequently overlooked roentgenologically in circumstances in which the roentgenologic consultant is supplied with inadequate clinical information.

The surgical procedure and 5 roentgenologic signs which can help confirm the presence of a radical neck dissection are described.

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HOW WAS THIS CHEST ROENTGENOGRAM TAKEN, AP OR PA?*

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THE question of whether a chest roentgenogram was obtained in the anteroposterior (AP) or the posteroanterior (PA) projection is occasionally important in its interpretation. Certain criteria, such as the location of an identifying marker or the use of a letter or number printed on the cassette screen, generally are sufficient for this determination. Sometimes, however, none of these landmarks can be utilized.

We have noted that the appearance of C6, C7, and T1 vertebrae will, in almost all instances, indicate the direction the roentgen-ray beam has traveled during the film exposure. In the anteroposterior projection, the body and joints of Luschka of these 3 vertebrae are well seen (Fig. 1). In the posteroanterior projection, however, the neural arch, articular processes, apophyseal joints, and laminae of these vertebrae are well delineated, while the body and joints of Luschka are not (Fig. 2). The spinous process of these vertebrae usually point upward in the posteroanterior projection.

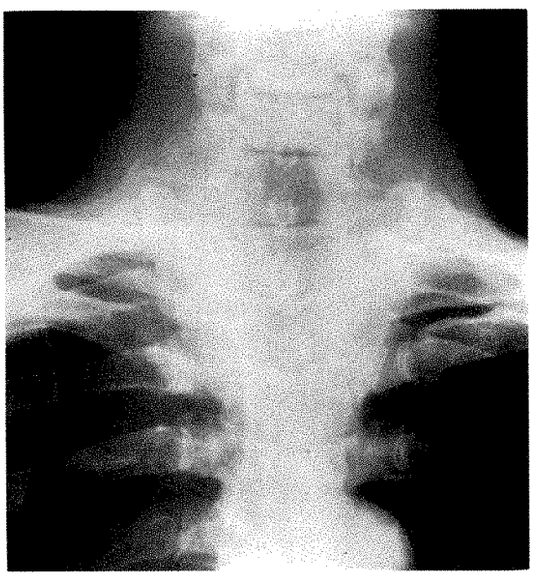


FIG. 1. Close-up, taken from an anteroposterior supine chest roentgenogram. The vertebral bodies of C6, C7, and T1 are well seen. The intervertebral disk spaces of the same vertebrae are well demonstrated as are the joints of Luschka.

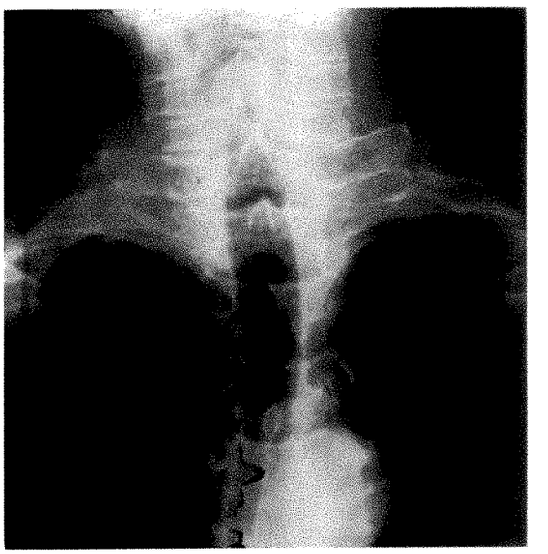


FIG. 2. Close-up from a posteroanterior upright chest roentgenogram. The C6, C7, and T1 articular processes and the apophyseal joints between them are clearly seen. The laminae and spinous processes point up.

The explanation for these findings is related to the divergent roentgen-ray beam and the anterior convexity of the cervical or upper thoracic column.[2] The bodies of the lower cervical vertebrae are tilted so that their upper surfaces face cranially and ventrally (Fig. 3). In the anteroposterior projection of the chest, particularly when a short target-film distance is used, the divergent roentgen-ray beam passes parallel

* Presented as a Scientific Exhibit at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
From the Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio.

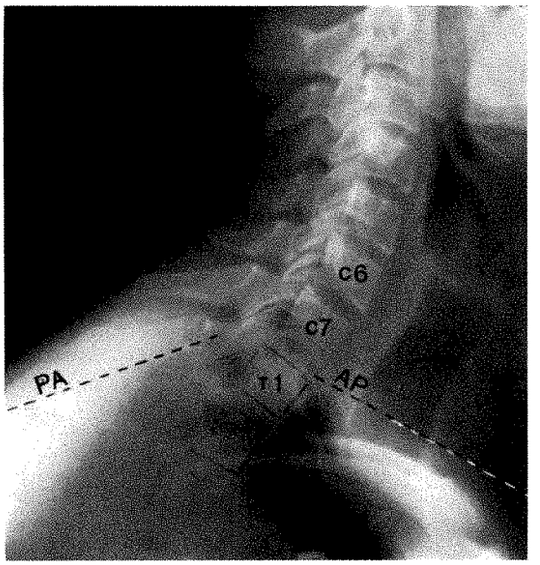


Fig. 3. Lateral roentgenogram of the cervical spine. The line AP corresponds to the direction of the beam in the anteroposterior position. The line also corresponds to the direction of the beam (15°–25° cephalad angulation) for examination of the cervical vertebral bodies. The line PA is in the same direction as the beam in the posteroanterior upright chest examination. This line in the opposite direction (namely the AP with caudal angulation of the tube) is used to examine the articular facets.

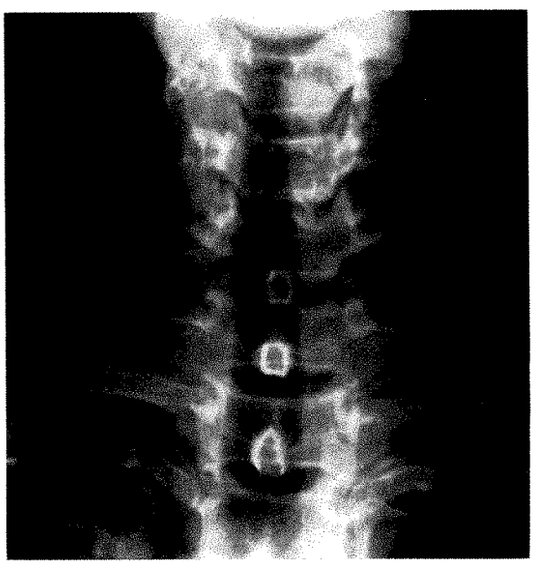


Fig. 4. Anteroposterior projection of the cervical spine with cephalad angulation of the tube. Compare with Figure 1.

to the upper surface of the vertebral bodies of C6, C7, and T1. Thus, a view similar to the widely used anteroposterior roentgenogram of the cervical spine with 20° cephalad tilt is obtained—a view designed to bring out the superior and inferior vertebral body plates, intervertebral disks, and the joints of Luschka[1,3,4] (Fig. 4).

In the posteroanterior projection of the chest, the diverging roentgen rays pass between the articular processes of these vertebrae, outlining them clearly. The roentgen appearance is similar to that obtained in an anteroposterior view of the cervical spine with 25° caudal angulation[1,3,4] (Fig. 5).

To test the validity of this finding, 100 chest roentgenograms, either anteroposterior or posteroanterior were randomly selected from our files. All portions of the film except for the lower cervical and upper thoracic area were covered and shown to 3

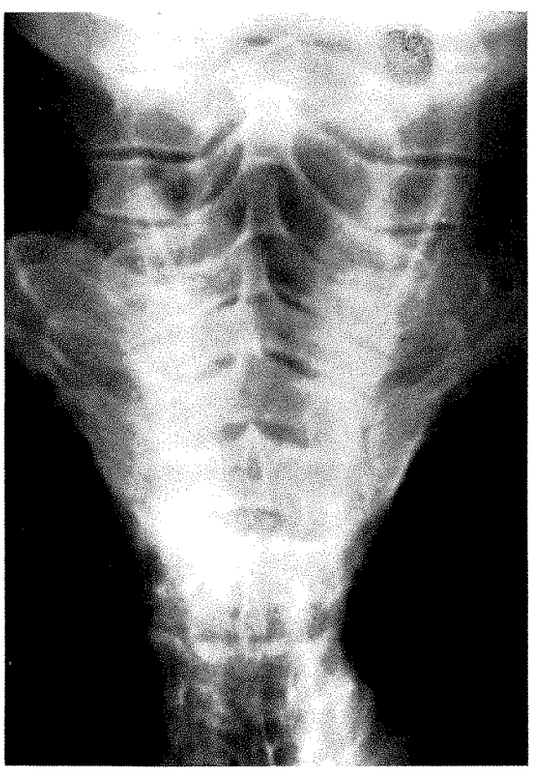


Fig. 5. Anteroposterior projection with caudad angulation of the tube. Compare with Figure 2.

radiologists and 2 senior residents, all of whom had been informed of the method beforehand. All examiners agreed and were correct on 78 films. In 6, all readers were in error or were unable to make a determination. In 15, 3 or 4 of the examiners were correct. In the remaining case, only 1 reader was correct.

It is evident from the foregoing that the signs are not infallible. In 5 of the 6 films in which all examiners were in error, the exposure had been taken in the anteroposterior projection. It is interesting that in all of these films, the patients had an abnormal degree of dorsal kyphosis. In the kyphotic patients whose chest roentgenograms were made in a posteroanterior projection, no such errors were made. Undoubtedly the additional cranial and ventral angulation of the vertebral bodies caused by the kyphosis contributed to errors in interpretation.

Roentgenograms of small children, those of patients with a straight dorsal spine, studies obtained with a long target-film distance, and those made with the tube centered high on the chest, may also cause difficulty in interpretation. If higher cervical vertebrae are used for interpretation, errors are made because of the variances in the angulation of these vertebrae.

SUMMARY

Evaluation of the appearance of C6, C7, and T1 on a chest roentgenogram may be of considerable help in determining the position of the tube and film at the time the exposure was made. Although the criteria are not infallible, they appear to be of significant reliability.

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OCCULT INFECTION OF ABDOMINAL INCISION AS SEEN ON LATERAL CHEST ROENTGENOGRAM*

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GAS was detected in upper abdominal wounds on the lateral chest roentgenograms of 4 patients evaluated for postoperative fever.

MATERIAL AND METHOD

Figure 1 shows a typical site for this finding in 1 of the patients. Two patients had right subcostal incisions and 2 had midline incisions. In all 4 instances, a portion of the wound was seen tangentially in the upper adbominal midline on the lateral chest roentgenogram. Figure 2, *A–D*, shows the relation of the areas of gas to the abdominal wall and viscera in the 4 patients.

Subsequent physical examination of these wounds gave minimal evidence of wound inflammation in 3 of the 4 patients. Two of these 3 were treated by incision with drainage of pus from the wound. The third patient was treated with antibiotics and the wound healed *per primam intentionem* with no proof of infection by culture.

In the fourth patient, no inflammation of the wound was evident locally. Bile peritonitis was suspected as the cause, however, of persistent deep tenderness and fever. Exploratory surgery was scheduled but because of the roentgenographic finding of subcutaneous gas in the midline (Fig. 2*D*), the medial portion of the wound was incised at bedside. The superficial wound was normal, but a pocket of pus and gas was discovered above the fascia in the area of roentgenographic abnormality. After drainage of the wound, the patient recovered. *Escherichia coli* was cultured from the wound drainage.

The abnormal gas in these wounds was noted on chest roentgenograms obtained 4 to 8 days postoperatively. Such wound gas after abdominal surgery, particularly in febrile patients, should strongly suggest the possibility of a wound infection, since postsurgical gas should be absorbed by this time.[3]

DISCUSSION

It is of great importance to note abnormal gas deposits on roentgenograms. Gas

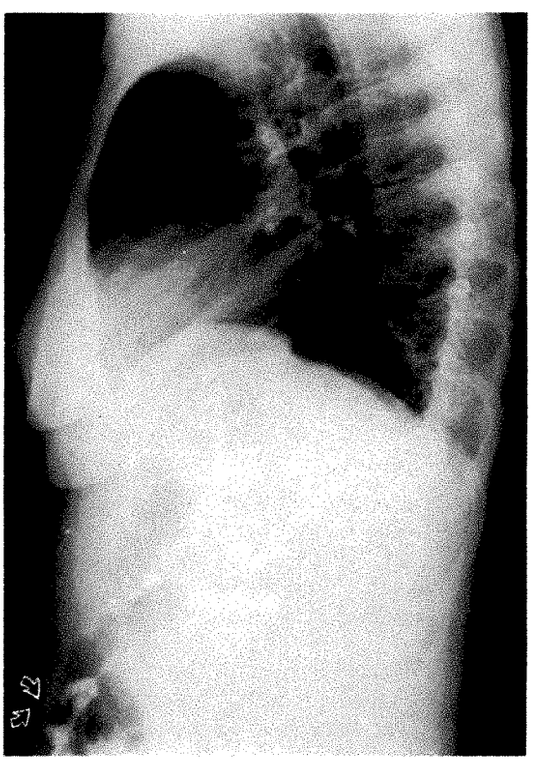


FIG. 1. Location of gas in the wound (arrows) in the upper abdominal midline as seen on a lateral roentgenogram of the chest.

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† Trainee in Veterans Administration Radiology Training Program.
Supported, in part, by Radiology Training Grant TR 136a from the Veterans Administration.

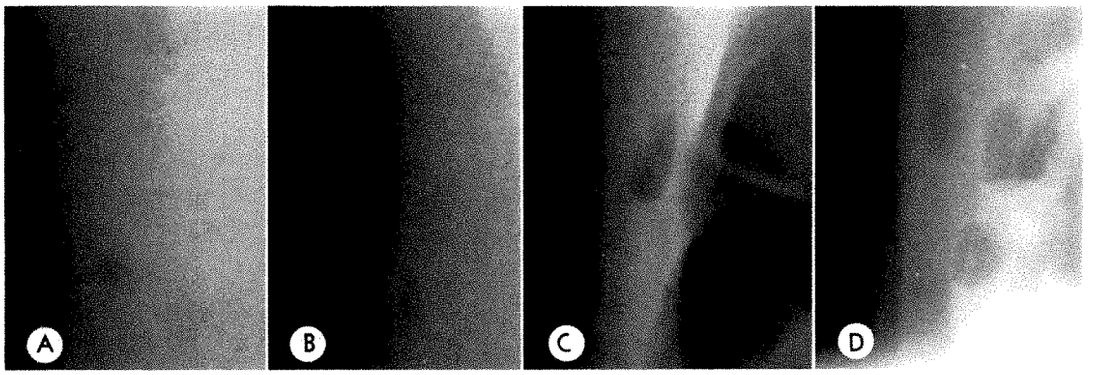


Fig. 2. (*A–D*) Appearance of gas in the wounds of the 4 patients as seen on lateral chest roentgenograms.

gangrene and trauma manifested in roentgenograms are well known.[3] Wound emphysema is common in patients who have undergone thoracotomy.[4] Persistence of intraperitoneal gas for as long as 2 weeks after laparotomy is also well documented.[1]

The presence of subcutaneous gas in a closed abdominal surgical wound implies local wound sepsis. In 3 of these 4 patients, incision and drainage of the wound yielded pus and, predominantly, *E. coli*, a potential gas-forming microorganism.[2] One patient did not have wound drainage but responded to systemic antibiotic therapy.

CONCLUSION

Since the lateral chest roentgenogram often shows a portion of upper abdominal surgical wounds tangentially, this area should be carefully observed in patients with fever following laparotomy. The roentgenologist may be the first person to observe objective evidence of wound infection.

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AN AUTOMATED SYSTEM FOR RECORDING REPORTS OF CHEST ROENTGENOGRAMS*

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EXAMINATION of the chest commonly forms the most frequent study in diagnostic radiology, making up about 45 per cent of adult radiologic examinations.[2,3] The detailed steps radiologists customarily carry out in reporting these films exact a significant toll from the potential efficiency of the procedure. A flow diagram (Fig. 1) combining structure and function of the conventional way of handling the interpretation of a chest roentgenogram depicts the separate acts involved.

In survey examinations of the chest, abdomen, stomach and breast, radiologists usually create various special ways to record their findings; through necessity, all adopt some type of an abbreviated reporting system. Most of these schemes omit registering every minor abnormality present. Instead, they utilize yes or no, normal or abnormal statements, either ignoring or leaving the reporting of seemingly nonsignificant, nonpertinent details to any standard examination. Since most radiologic surveys accept limited medical objectives and often use small, cost-saving films and assembly line production methods, demanding reasons for a shortened approach to handling radiologic diagnosis can be found. The clearly superior diagnostic quality of the life size roentgenogram has led recently to the wider use of this film in various chest screening programs. Whether large or small films are employed, the introduction of modern recording procedures and equipment can make feasible full, initial reporting of all abnormalities no matter the objective, be it survey or standard examination.

When reporting routine or survey chest roentgenograms as negative, some radiologists have used a predictated, automatically typewritten form consisting of one or more statements. Yet our experience, based upon approximately 26,000 examinations of

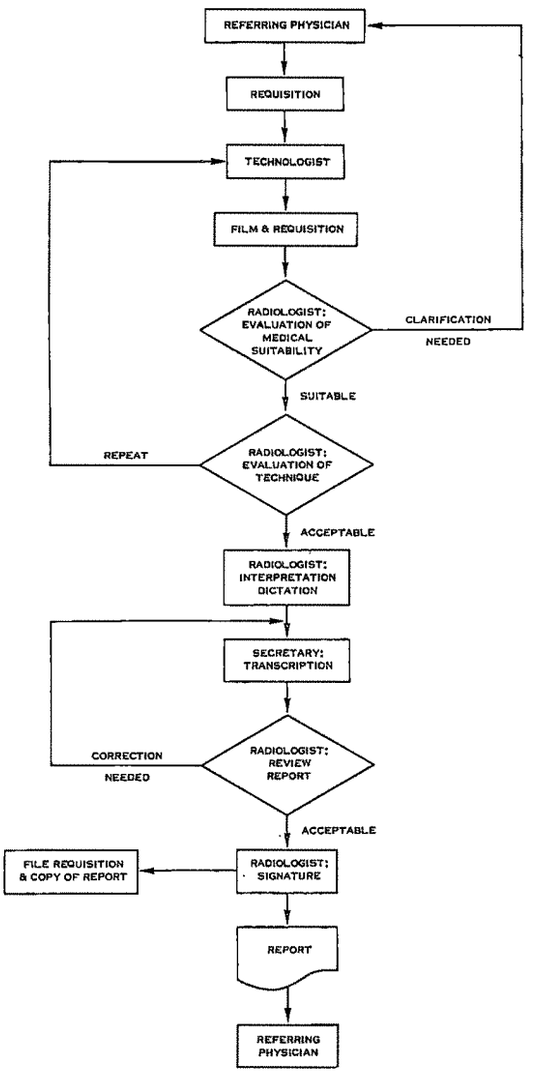


FIG. 1. Customary system of reporting a chest roentgenogram.

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† Corporate Consultant in Radiology, Medical Department, International Business Machines Corporation, Armonk, New York.

presumably healthy workers, showed that even in this kind of survey, completely negative chest roentgenograms made up only 64 per cent of the total. The remaining (36 per cent) demonstrated either nonsignificant (29 per cent), or possibly significant abnormalities (7 per cent). Consequently, healthy workers, individuals seemingly less likely to have abnormalities, will present reportable findings in 1 out of 3 chest examinations. The use of any sort of an automated negative report, while serving the majority, nevertheless would require either ignoring many defects or describing them in the conventional way, *i.e.*, by a dictated, narrative report. Compelling medical reasons exist against ignoring such seemingly nonsignificant findings. Their importance in teaching and in statistical comparative and prognostic studies seems clear, while their potential significance to the patient's health at present or in the future requires careful clinical judgment in addition to the radiologic one.

If describing chest roentgenograms fully by conventional methods becomes cumbersome for survey work, to do so for many routine, standard examinations seems equally inefficient. Desirable objectives to be gained by improving standard reporting methods would be to save the radiologist's time, cut back substantially on secretarial and related costs, eradicate as many chances for errors and misunderstandings as possible and, especially, to shorten the time between the roentgenologic examination and the delivery of the report. If, at the same time, the radiologist's findings were presented on a form designed to be both requisition and report, readable in its original form as well as processable by an optical device for either "on-line" or batch computer processing, major advantages would accrue.

MARK-SENSE SYSTEM*

In order to accomplish these objectives we obtained several types of computer analyses of the reports of approximately 26,000 chest roentgenograms on employees. Based upon these computer data which included a word frequency count, and experience in interpreting these films, we devised and have thoroughly tested a combination mark-sense requisition and report (Fig. 2). The referring physician or his agent fills out the first part of this form. The line, "reviewed by," is filled in by the referring physician in accordance with existing medical department procedures. The radiologist blacks out each appropriate diagnostic item as he views the film. An optical page reader then processes the sheet. This machine converts all identifying and diagnostic data to codes which are automatically punched into a card. The computer then processes the card translating the codes into corresponding statements (Fig. 3). The end result is a computer printed narrative report in the customary format covering fully both the negative (64 per cent) and the nonsignificant findings (29 per cent). In the former category the statement "General Findings: Within normal limits," constitutes the opinion.

This mark-sense sheet has eliminated approximately 60 per cent of the typist's work by volume and about 90 per cent by number of individual reports. A flow chart (Fig. 4) indicates how much this system shortens and improves on the customary procedure without slighting any of the requirements of good radiologic practice. Because the radiologist, himself, marks a number which identifies him on the report and because mistakes in spelling and typing and omissions cannot occur, he removes the need for later reviewing his report and signing it. The system includes a computer edit step prior to printing the report which ensures that all required information has been supplied and that any inconsistencies are brought to light.

Another major advantage attaches to this system. With survey programs in particular, and in all general radiologic work, maintaining high technical quality holds

* The equipment used in this system consists of the IBM 1232 Optical Page Reader, IBM 1800 and IBM 360/65 computers.

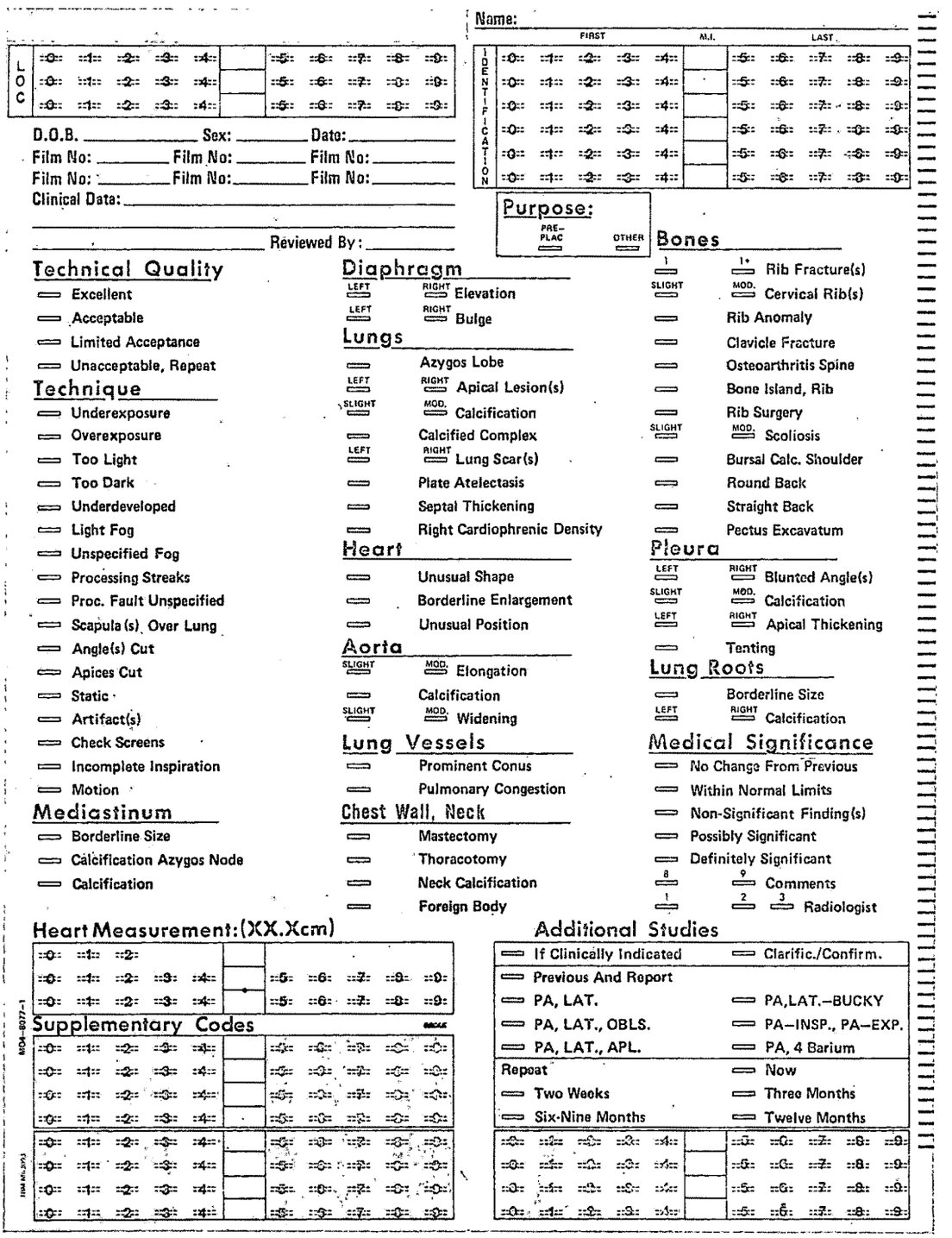


Fig. 2. IBM report of a chest roentgenogram.

prime consideration. By using this method, the radiologist renders an immediate and detailed quality rating on each film for the guidance of the technologist who made the roentgenogram. This information also goes into the computer which tabulates and prints it in periodic reports. These evaluations made individually, and consolidated periodically to indicate trends (Fig. 5) provide an effective means over short and long periods of time for evaluating and controlling the quality of the work of our technicians working in many different radiologic installations.

To separate the negative from the 2 other major diagnostic categories, nonsignificant and possibly significant, holds no problem for the radiologist. When making the decision for a negative report he simply indicates that he finds nothing whatsoever in the chest roentgenogram which can be considered abnormal. In any instance of doubt, the examiner would then use whichever description seemed the more appropriate, nonsignificant or possibly significant. Although a fourth category, definitely significant, appears on the present requisition report form, we have not needed to use it.

Distinguishing radiologically between a nonsignificant and a possibly significant abnormality constitutes neither as arbitrary nor as binding a medical opinion as might appear at first glance. Should any question arise as to the correct choice between the diagnostic categories, nonsignifi-

There is calcification of the azygos node.

The left hemidiaphragm is elevated slightly.

There are minimal lesions in the left lung superiorly.

A calcified complex is present.

The heart shape is a little unusual.

The aorta shows slight elongation.

A breast operation has been performed.

There are small cervical ribs.

There is an old clavicular fracture.

The thoracic spine shows moderate scoliosis.

There is blunting of the left costophrenic angle.

Fig. 3. A sampling of statements, corresponding to the relevant, nonsignificant, diagnostic items on the check sheet.

Sherman

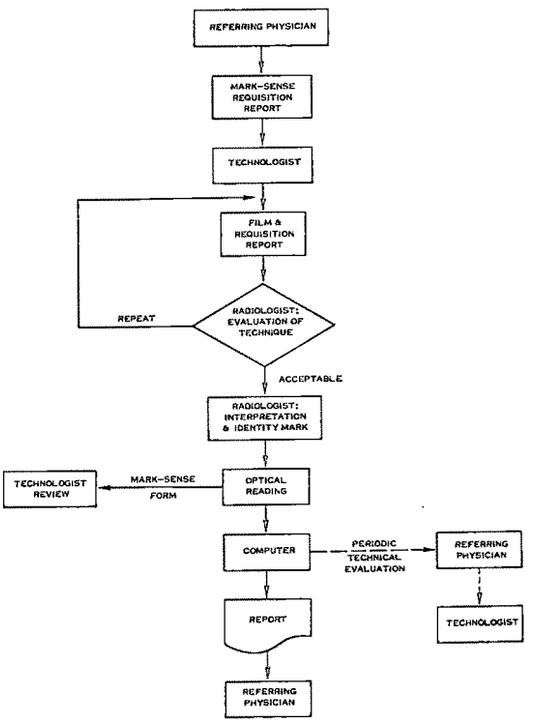


Fig. 4. Present system of reporting a chest roentgenogram.

CATEGORY	FOR THE PERIOD 09/69 TO 02/70		FOR THE PERIOD 03/70 TO 05/70	
TECHNIQUE				
EXCELLENT	29	6.%	5	2.%
ACCEPTABLE NO FAULTS	246	57.%	75	35.%
ACCEPTABLE W/FAULTS	146	34.%	121	57.%
ACCEPTABLE-LIMITED	7	1.%	11	5.%
TECHNICAL FAULTS				
MOVEMENT	0	0.%	0	0.%
POSITIONING	36	8.%	7	3.%
FOG	3	0.%	1	0.%
STATIC	6	1.%	0	0.%
FOREIGN OBJECTS	0	0.%	0	0.%
ARTEFACTS	1	0.%	1	0.%
ACCESSORIES	0	0.%	0	0.%
IDENTIFICATION	0	0.%	0	0.%
DEFICIENT DATA	0	0.%	0	0.%
OTHER	0	0.%	0	0.%
PROCESSING	0	0.%	0	0.%
EXPOSURE	105	24.%	123	58.%
TOTAL FAULTS	153	35.%	132	62.%
TOTAL	428		212	
TOTAL UN-ACCEPTABLE FILMS	———		———	

Fig. 5. A quarterly technical control report for one radiologic unit. IBM Medical Data Center. Total roentgenograms 428 and 212 for the 2 periods, respectively.

cant and possibly significant, we always select the second. Referring physicians continue to enjoy their prerogative of being free to accept or reject the radiologist's judgment in this matter. Our experience in dealing with a score or more of physicians indicates no controversy. Since the referring physician receives a specific statement about every abnormality, he can relate each defect to the clinical setting and judge its diagnostic significance himself. To help in this matter he usually has the film as well as the report.

Until a satisfactory thesaurus with codes or a system of structured language to handle the description of all possibly significant findings can be developed,[6] we continue to use conventional methods of dictation for 7 per cent of the examinations. Should there be nonsignificant defects in addition to the possibly significant ones, they need not be referred to in the dictation. They are recorded in the report by making the appropriate marks on the requisition report sheet, thus lessening the typist's work. In the situation referred to, the medical significance section of the mark-sense sheet would be marked "Possibly Significant as well as "Comments." The dictation must be made to integrate clearly and logically with statements on any nonsignificant findings generated by the mark-sense sheet.

The section "Supplementary Codes," on the mark-sense sheet provides for special coding up to 3 separate diagnoses. To use this facility we devised a simple classification to make retrieval of any possibly significant diagnostic data easier and more reliable than having to utilize a computer word search. We simply enter a 4 digit code number, the first half of which corresponds to the anatomic part or body system involved and the second to the suspected nature or etiology of the abnormality. By this approach we can be as specific or as general in our diagnostic codings as each situation warrants.

When either the 8 or the 9 is blacked out in the "Comments" area of the mark-sense sheet, the computer, as well as anyone reading the completed sheet, is alerted to the existence of the dictated part of the report. Marking either 8 or 9 serves our special purpose; to divide all possibly significant diagnoses into the noncardiovascular, 9, on the one hand and the cardiovascular, 8, on the other, accompanied or not accompanied, as the case might be, by additional noncardiovascular findings.

When previous roentgenograms are submitted for comparison with the current chest roentgenogram, their identity is entered by the referring source in the spaces provided. If there have been earlier reports and no change has occurred in the findings since the last examination, the sheet is checked "No Change From Previous," and the previous diagnostic designation, either "Within Normal Limits," "Nonsignificant Findings" or "Possibly Significant" is also marked. The section, "Additional Studies," on the mark-sense requisition report seems self-explanatory.

A capability we plan to implement allows the radiologist to make the computer calculate and print the cardiac size. The method of mensuration we selected provides a more accurate appraisal of cardiac enlargement than the cruder, commonly used ratio of transverse diameters of the heart and thorax.[1] To trigger this automated response, the radiologist fills in the measurement of the transverse cardiac diameter as determined directly from the film, or to save time he can simply mark with a wax pencil the outer-most points of the right and left cardiac borders. Later an assistant measures between these dash marks and fills in the value on the sheet in the heart measurement box. Because the height and weight of individuals roentgenographed have been entered in the computer, the machine can determine from the charts of Ungerleider and Clark[5] the cardiac size as a percentage deviation from the predicted normal. An investigation we have completed demonstrates that the standard chest roentgenogram uncovers a significant number of workers with negative electro-

cardiographic reports who have heart enlargement.[4]

DISCUSSION

This mark-sense system, by segregating a major part of the total reporting load into normal and nonsignificant categories, permits rapid automated handling of these cases in a way that coincides with, indeed, actually reinforces the diagnostic radiologist's search and thought processes. It also constantly reminds him of the range of his responsibilities and encourages a systematic evaluation of each anatomic part and body system shown on the film. It necessitates intermittent scanning of the roentgenogram by requiring a momentary looking away from the film to record data on the check sheet. This brief maneuver, a kind of second look, seems to improve visual search and detection.

This method does not compromise in any way the customary, satisfactory physical setting for film interpretation. The handling of the films, and the use of a foot control with a desk or neck microphone on the recording device makes dictation on the possibly significant cases easy to integrate with the use of the mark-sense sheet. When we compared the radiologist's dictating speed with this system with the conventional method of reporting all cases into a recording device we found the former just as rapid.

The ultimate step in this automated method of chest film reporting would be the development of some sort of thesaurus with numbers to record descriptively and diagnostically the possibly significant findings. Short of this ideal, structured dictation seems indicated.

We have investigated the problem of diagnostic codes sufficiently to convince ourselves that no single system will satisfactorily serve the needs of all radiologists, many of whom must deal with different types of patients and various clinical disorders. The lack of any generally accepted radiologic classification after years of effort and several officially sponsored systems supports this opinion. For example, in our experience, standard coding systems of radiologic diagnoses have serious drawbacks for oncologic material. They also seem too cumbersome for survey and industrial radiology. We believe that a radiologist working in an orthopedic or a pediatric hospital would probably do best by developing his own coding system to satisfy his particular requirements. But whatever system the individual radiologist does devise, it should in turn be readily convertible to other standard classifications whenever the need arises.

SUMMARY

Based upon an experience with approximately 26,000 "apparently healthy" workers, an automated, computerized mark-sense system for recording the radiologist's findings in the negative and nonsignificant diagnostic categories for the chest examination has been devised and tested.

The system, while faster and easier and more reliable than conventional reporting, is far more efficient than the customary method of reporting chest roentgenograms. In addition, it provides for the integration of any dictated material with any nonsignificant diagnostic items being automatically recorded. This system also includes methods for immediate and long range quality control of roentgenographic technique.

Computer determination of the percentage deviation from normal heart size as based upon height-weight standards can be easily initiated by the radiologist using this system.

The application of this system to other types of radiologic examinations could be easily arranged.

We believe that no single radiologic diagnostic code or classification can most satisfactorily serve the needs of all radiologists; yet, all systems should be interrelated.

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tor, and the technical contributions of several members of the IBM staff.

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CERVICO-MEDIASTINAL THYMIC CYSTS*

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THYMIC cysts are relatively rare, most commonly asymptomatic, benign lesions, which roentgenographically may present as cervical or anterior mediastinal masses. Due to their infrequency, accurate preoperative diagnosis is seldom made.

The purpose of this paper is to present 3 cases with thymic cysts, one of which is the first American case in which ultrasonography played a major role in diagnosis and management. The salient ultrasonographic as well as the embryologic, clinical and roentgen features of thymic cysts will be discussed.

EMBRYOLOGY

The primordia of the thymus gland originate from the paired ventral sacculations of the third pharyngeal pouches at approximately 6 weeks of intrauterine life. The lumina of these tubular structures rapidly become obliterated by epithelial proliferation. At the eighth week of fetal life, these paired solid bars unite inferiorly in the midline and attach to the pericardium during its caudal descent into the anterior mediastinum. Remnants of thymic tissue may be pinched off and left along the cervical path during the course of migration.

REPORT OF CASES

CASE I. L.R., 22 year old Puerto Rican male, was admitted because of an anterior neck mass. The sole abnormality on physical examination was a large, bilobed cystic mass at the base of the neck.

A thyroid scan was normal. Chest roentgenograms showed a huge multilobulated cervico-mediastinal mass (Fig. 1, *A* and *B*).

Ultrasonography (Fig. 1, *C* and *D*) showed the lesion to be cystic. Puncture of the cervical extension of the mass with contrast material injection (Fig. 1*E*) revealed 2 loculated cystic compartments with no apparent communication with the mediastinal mass. Aortography showed that the entire mass was avascular (Fig. 1*F*).

At surgery, a 20×16×10 cm. cystic, multiloculated mass in the anterior mediastinum extending to the superior mediastinum, thoracic inlet and base of the neck, was resected.

Microscopic sections revealed a fibrotic cyst wall with segments of thymic tissue containing partially calcified Hassall's corpuscles. The pathologic diagnosis was cervico-mediastinal thymic cyst.

CASE II. R.S., 70 year old white female, was admitted to BJH for removal of a large mediastinal mass which had been present for many years. The patient had complained of episodes of dysphagia, dyspnea and anterior chest wall pressure which had increased during the last few months.

Except for a pectus excavatum deformity, physical examination on admission was within normal limits. The neck veins were not distended. Urinalysis and a hemogram including electrolytes were normal.

Chest roentgenograms revealed a right paracardiac mass (Fig. 2, *A* and *B*).

At surgery, a large cystic structure, measuring 10×5×5 cm., filled with clear fluid, was found adjacent to the pericardium and anterior to the medial aspect of the lung. It was freely separated from the pericardium and appeared to be loosely attached to the retrosternal region.

Microscopic sections revealed a thin cyst wall lined by low cuboidal epithelium. The pathologic diagnosis was thymic cyst.

CASE III. M.V., 32 year old Puerto Rican female, was admitted complaining of mild left upper chest pain which was aggravated by coughing. A left hilar mass had been noted elsewhere on a routine chest roentgenogram 3

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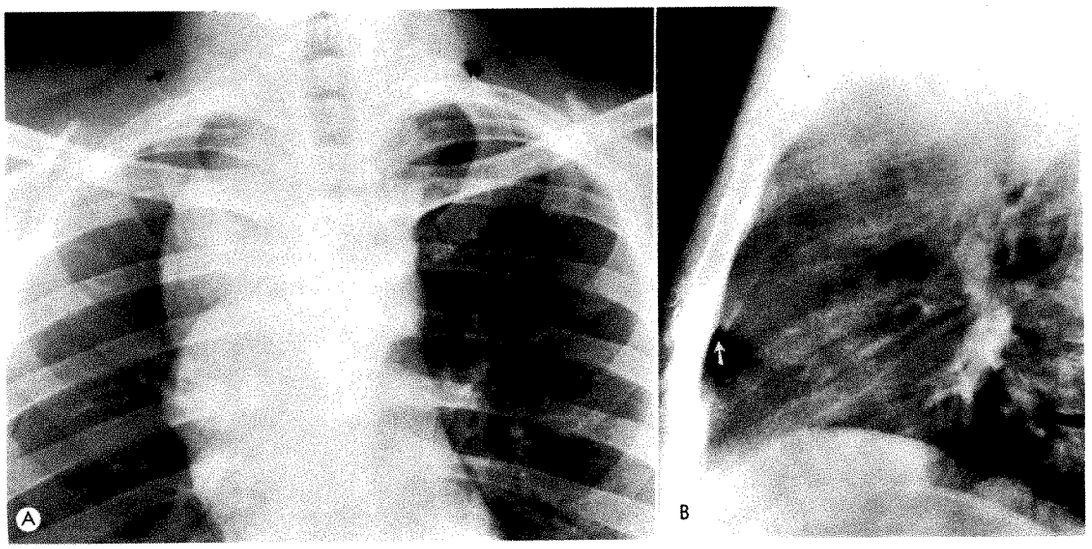


Fig. 1. Case 1. (*A*) Frontal chest roentgenogram shows a large lobulated mediastinal mass with cervical extension (arrows). (*B*) Lateral roentgenogram shows the mass to be anteriorly situated. Note inferior sulcus (arrow) suggesting thymic origin of the lesion.

months prior to admission, but she had refused surgery.

The current physical examination was within normal limits.

Chest roentgenogram on admission showed a left hilar mass (Fig. 3*A*), which rapidly increased in size as noted on the follow-up roentgenogram taken 3 days later (Fig. 3*B*). The lateral chest roentgenogram (Fig. 3*C*) suggested a thymic lesion. Angiography (Fig. 3*D*) revealed the mass to be extravascular.

A left thoracotomy was performed and a pre-

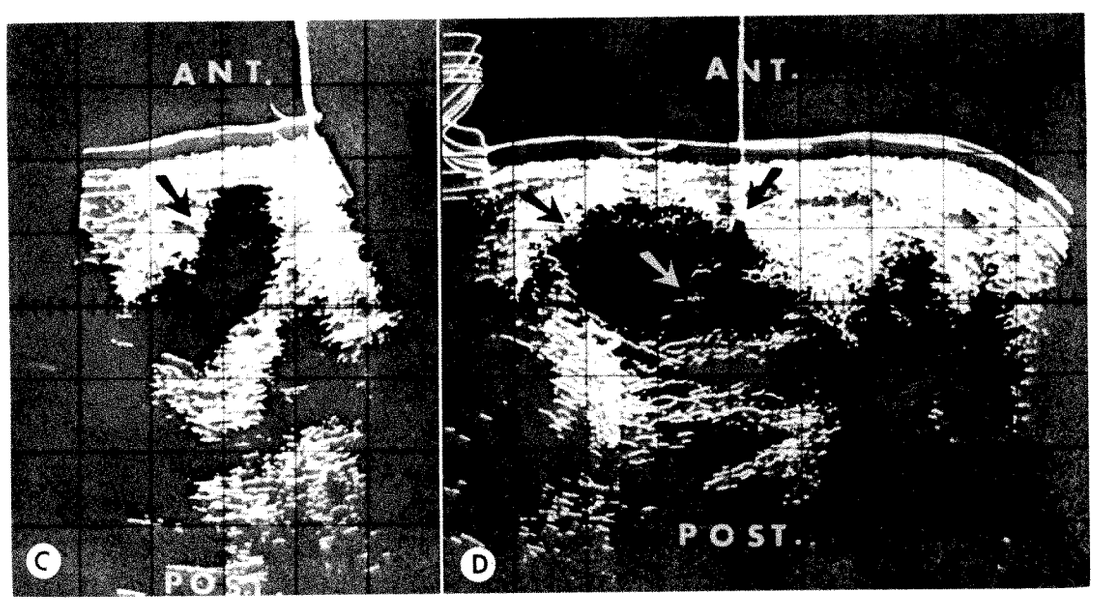


Fig. 1. (*C*) B-mode ultrasonogram, transverse scan of base of the neck. Note cystic neck mass (arrow). (*D*) B-mode ultrasonogram, transverse scan, at level of 3rd anterior intercostal space. Note cystic mediastinal mass (black arrows). Intracystic echoes (white arrow) probably reflect debris.

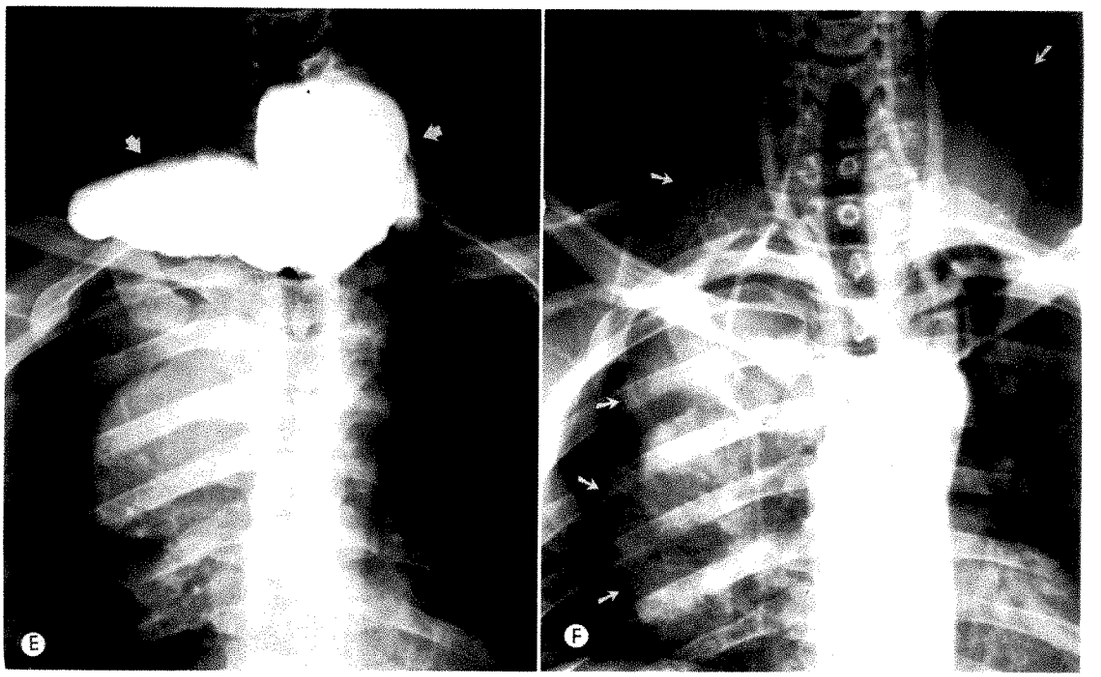


FIG. 1. (*E*) Cyst puncture. Note contrast material outlining the cervical portion of the large loculated cyst (arrows). There is failure of the mediastinal compartment to fill with contrast material. (*F*) Aortogram outlining an avascular mass (arrows) unrelated to the cervico-mediastinal vasculature.

dominantly left-sided anterior mediastinal mass containing serosanguineous fluid was excised. The pathologic diagnosis was "thymic cysts with hemorrhage."

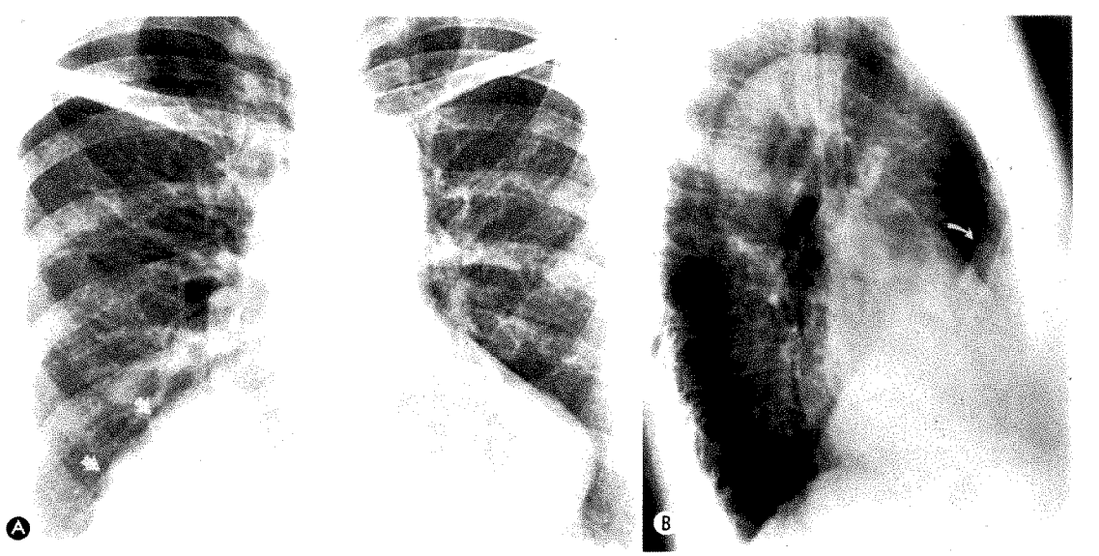


FIG. 2. Case 11. (*A*) Posteroanterior and (*B*) lateral chest roentgenograms demonstrating a right paracardiac mass blending with the right cardiac border (arrows in *A*). Its tear-drop shape is suggestive of a cystic or lipomatous mass. The lateral view reveals its pedunculated attachment to the anterior mediastinum (arrow in *B*).

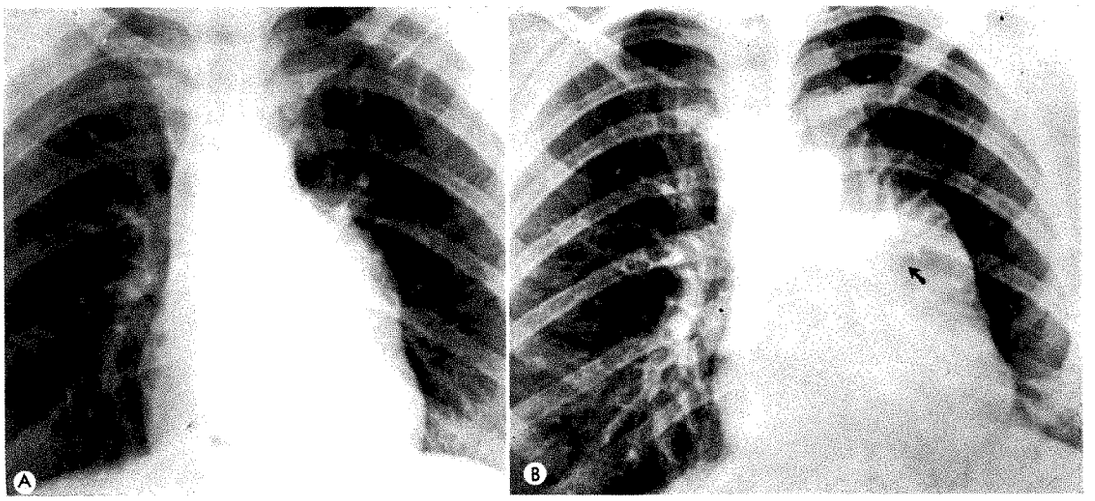


Fig. 3. Case III. (*A*) Frontal chest roentgenogram shows a left-sided lobulated paracardiac mass. (*B*) Three days later. Frontal chest roentgenogram demonstrates the rapid enlargement of the mass suggesting intracystic hemorrhage. Note the presence of hilum overlay (arrow).

ROENTGENOGRAPHIC FEATURES

Roentgenographically, thymic cysts present as well demarcated soft tissue anterior mediastinal or cervical masses, rarely bridging both locations. They are most often lobulated and of variable size with rapid increase in size usually indicative of intracystic hemorrhage[13,21] (Case II; Fig. 2, *A* and *B*).

Extrapleural localization, as indicated by a sharply demarcated mass abutting adjacent lung, is commonly observed. On frontal chest roentgenograms the cyst may blend with or be lost well within the cardiac silhouette due to its anterior location[7] and may occasionally simulate cardiomegaly or pericardial effusion.[2,19] Due to its proximity to the heart and great vessels, transmitted pulsation may be observed fluoroscopically. Demonstration of hilum overlay or hilum convergence on a well penetrated chest roentgenogram will suggest the extravascular location of the lesion.[7] Angiography serves to confirm its independence

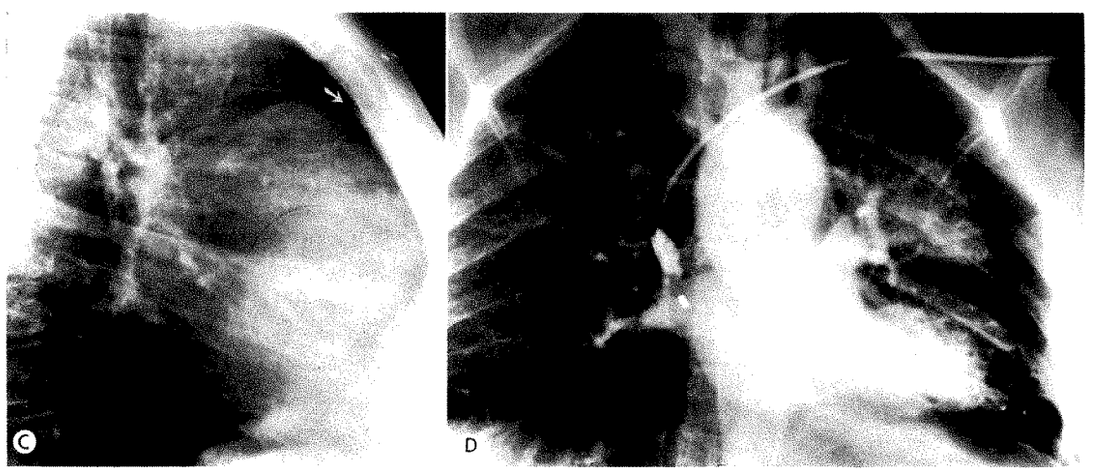


Fig. 3. (*C*) Lateral chest roentgenogram demonstrating the presence of a superior sulcus suggesting a thymic lesion (arrow). (*D*) Angiocardiogram shows the lesion to be extravascular.

from the great vessels and to demonstrate its avascularity. The presence of a sulcus at the margin of the lesion on the lateral chest roentgenogram suggests a thymic lesion.[10] This is well demonstrated in Case I (Fig. 1*B*) and Case III (Fig. 3*C*). Arcuate calcification of the cyst margin may occasionally be observed.

Cyst puncture and aspiration, particularly in the readily accessible cervical region, with introduction of radiopaque contrast material may help delineate the lesion's extent and demonstrate its frequently multiloculated nature (Case I; Fig. 1*E*).

ULTRASONOGRAPHY AND DIFFERENTIAL DIAGNOSIS

The differential diagnosis of thymic cysts includes thymomas, teratomas, pericardial cysts, aneurysms, vascular tumors, malignant lymphomas, metastatic lymphoadenopathy, cystic hygromas, hydatid cysts, thyroid and parathyroid adenomas. Ultrasonography may play an increasingly important role in serving to establish the cystic nature of the lesion. If a cystic mass is demonstrated ultrasonographically (Fig. 1, *C* and *D*), it will practically exclude the numerous, predominantly solid masses previously alluded to and may then be followed by cystography, another useful, simple and confirmatory diagnostic test (Fig. 1*E*).

Thymomas may additionally be differentiated from thymic cysts in view of the former condition's frequent association with myasthenia gravis[4] and in a small minority of cases with refractory anemia.[18] Arteriography may delineate a prominent thymic artery and tumor blush associated with thymomas,[6] or an avascular mass in the case of thymic cysts (Fig. 1*F*; and 3*D*). Aneurysms and vascular tumors will usually be well outlined by angiocardiography.[5]

Thyroid adenomas and cysts may be differentiated from thymic cysts by means of radioiodine (I^{131}) uptakes followed by scanning.

Parathyroid adenomas may be frequently demonstrated by means of Se^{75} selenomethionine scan.[9]

Hydatid cysts may be suspected with a history of exposure in an endemic area and by a positive Casoni test.

Cystic hygromas and pericardial cysts, however, may have an identical roentgen appearance and their differentiation from thymic cysts may be exceedingly difficult.

CLINICAL FINDINGS AND DISCUSSION

Thymic cysts are rare, with most cases discovered early in infancy. In asymptomatic adults they may occasionally be incidentally detected as a mediastinal mass on routine roentgenograms or as a neck mass on physical examination.[20] Rarely, symptoms of chest pain, dysphagia, or hoarseness may develop. These findings are most frequently associated with intracystic hemorrhage.[1,13,21]

Our 3 cases occurred in adults, with cervico-mediastinal presentation in 1 case (Case I) and with primary mediastinal presentation in 2 cases (Cases II and III).

Plain roentgenograms usually demonstrate an anterior mediastinal mass, while angiocardiography confirms the presence of an avascular mass which receives no identifiable feeding vessels and merely displaces the surrounding normal vasculature (Fig. 1*F*; and 3*D*).

Ultrasonography appears to be of great value in establishing the cystic nature of the lesion. The technique is particularly feasible in terms of the location of the mass. Since the cysts are usually based in the anterior mediastinum, ultrasonography is not hindered by interposed lung tissue (Case I; Fig. 1*D*). The cysts are likewise located superficially in the neck and are readily delineated by means of ultrasonography (Case I; Fig. 1*C*). When ultrasonography has established the cystic nature, and angiography has excluded a vascular mass (Case I), cystography may further serve to complement and confirm the findings.

SUMMARY

Three cases with thymic cysts are presented, 1 of which is the first American case in which ultrasonography played a major role in diagnosis and management.

Ultrasonography is advocated as a valuable procedure in the safe and simple investigation of cervical and anterior mediastinal tumors.

The use of angiography and cystography as complementary techniques in the diagnosis of these tumors is outlined.

The embryology, clinical and roentgen findings of thymic cysts as well as their differential diagnosis are discussed.

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THE RETROSTERNAL LINE*

A NEW SIGN OF AN ANTERIOR MEDIASTINAL MASS

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THE roentgenographic evaluation of the retrosternal area many times presents a difficult problem. The normal anatomic structures cast confusing shadows. A radiodensity frequently seen anterior to the heart has been ascribed to the density of transverse thoracic muscle and, on occasions, to disease.[2] In addition, we have noticed with anterior mediastinal masses, particularly thymomas, a line which we could not find described previously in the radiologic literature. The mechanism for the production of this line is somewhat analogous to that of the normal density seen anterior to the heart shadow, and the anatomic explanation for both is the subject of this report. We have termed this the retrosternal line.

As in any area of Radiology, a thorough knowledge of the anatomy is the key to the

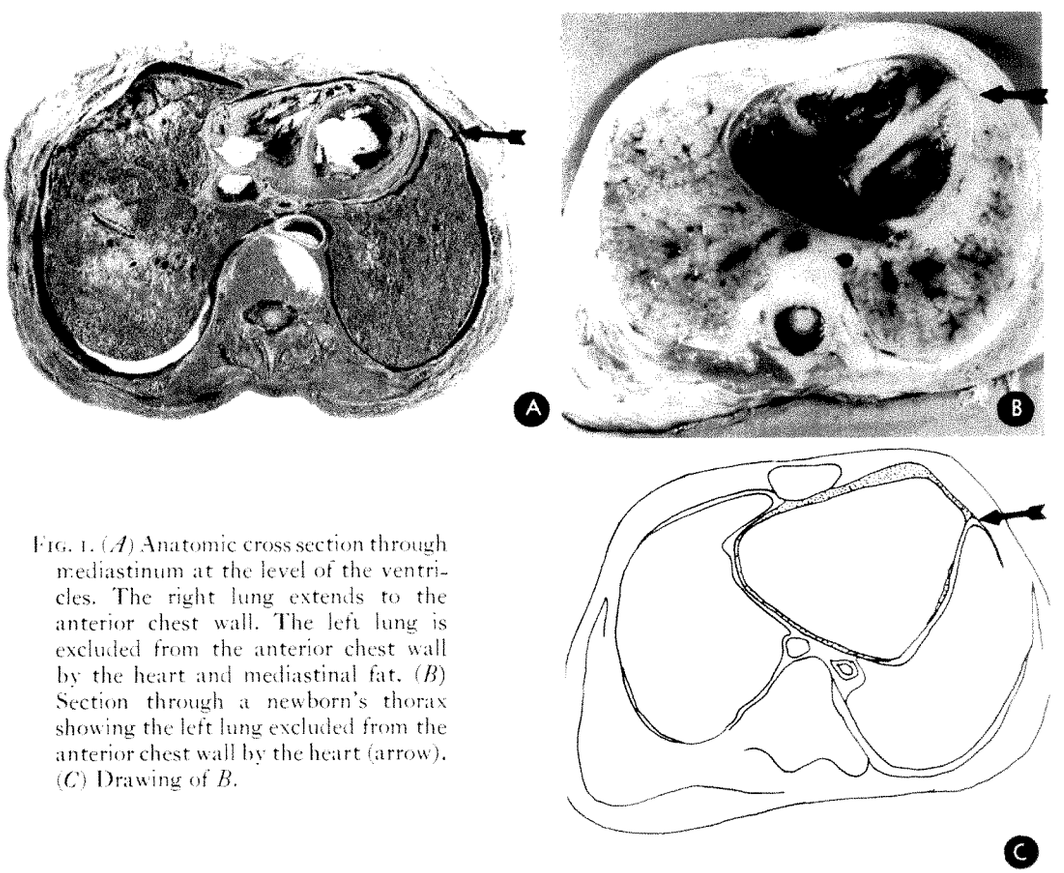


FIG. 1. (*A*) Anatomic cross section through mediastinum at the level of the ventricles. The right lung extends to the anterior chest wall. The left lung is excluded from the anterior chest wall by the heart and mediastinal fat. (*B*) Section through a newborn's thorax showing the left lung excluded from the anterior chest wall by the heart (arrow). (*C*) Drawing of *B*.

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
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This investigation was supported by the James Picker Foundation on recommendation of the Committee on Radiology, National Academy of Science, National Research Council.

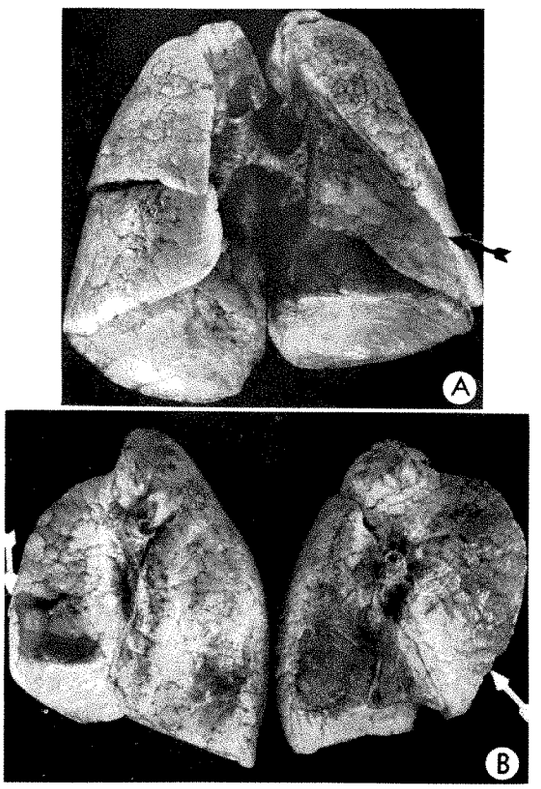


Fig. 2. (*A*) Frontal and (*B*) medial surfaces of inflated lung. The right lung is complete to the midline and has a smooth contour. No muscle indentation is seen. The left lung is deficient anterior (cardiac incisura) (arrow). (Courtesy of Dr. James McCort, San Jose, California.)

roentgen appearance, normal and abnormal. Because of the difficulty in explaining the normal roentgen images of this area and correlating the pathologic alteration, a detailed anatomic study of both the child and adult was undertaken. In addition, clinical roentgenograms of the mediastinal structures were carefully analyzed. The results of this study are herein reported.

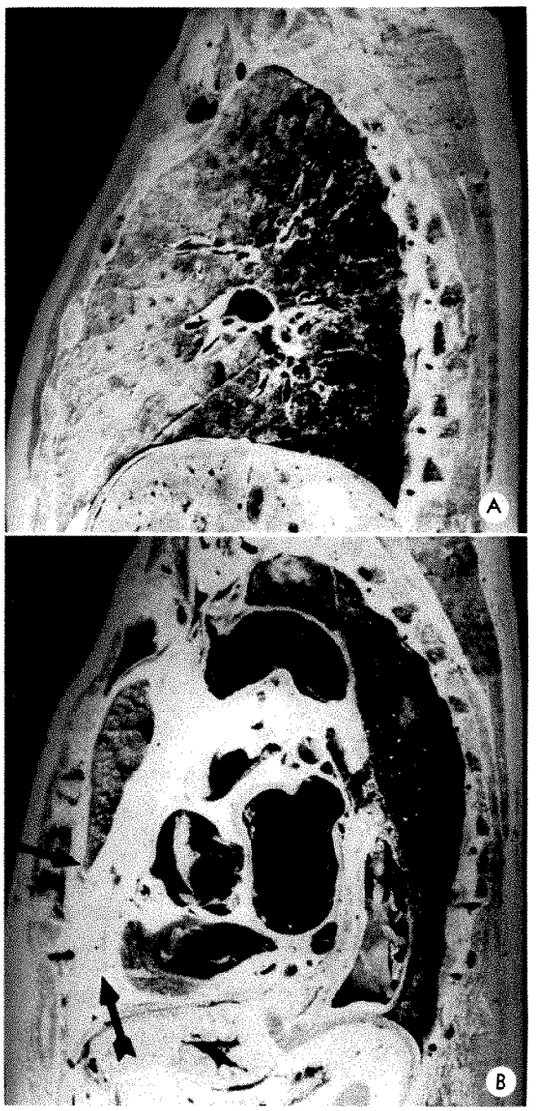


Fig. 3. (*A* and *B*) Sagittal sections of thorax. (*A*) Right of midline. The right lung is intimate with the anterior chest wall. No muscle indentation is seen, merely the smooth lobulation corresponding to the inner thoracic contour. (*B*) Left of midline. The lung is replaced by the heart and mediastinal fat. The pericardium (lower arrow) is contrasted by the pericardial and mediastinal fat.

Fig. 5. (*A*) Lateral roentgenogram showing a portion of the cardiac incisura separate from the shadow of the right lung. (*B*) An oblique lateral roentgenogram placing the left chest more posteriorly, separating the anterior surfaces of the right and left lungs—the right lobulated and complete to the anterior chest wall from top to bottom, the left deficient at the level of the heart (cardiac incisura).

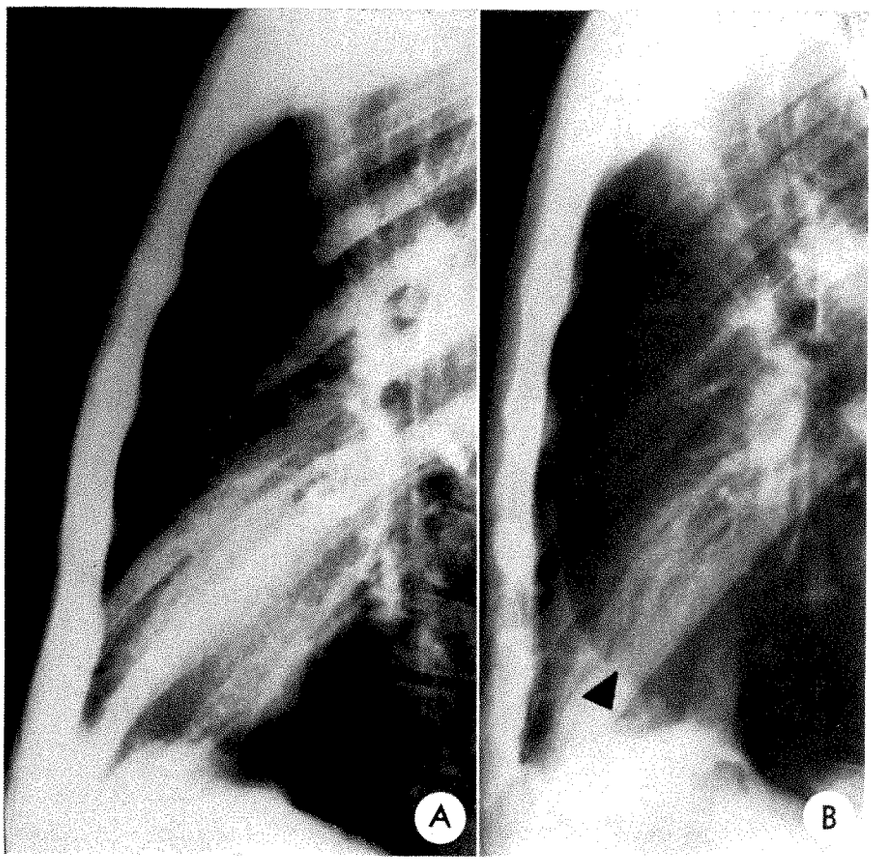


FIG. 4. (*A*) Lateral roentgenogram of the chest showing clear retrosternal area and the ill-defined heart shadow. (*B*) Slightly lordotic lateral chest roentgenogram "picking up" the interface of anterior left lung (arrowhead) and the mediastinal fat.

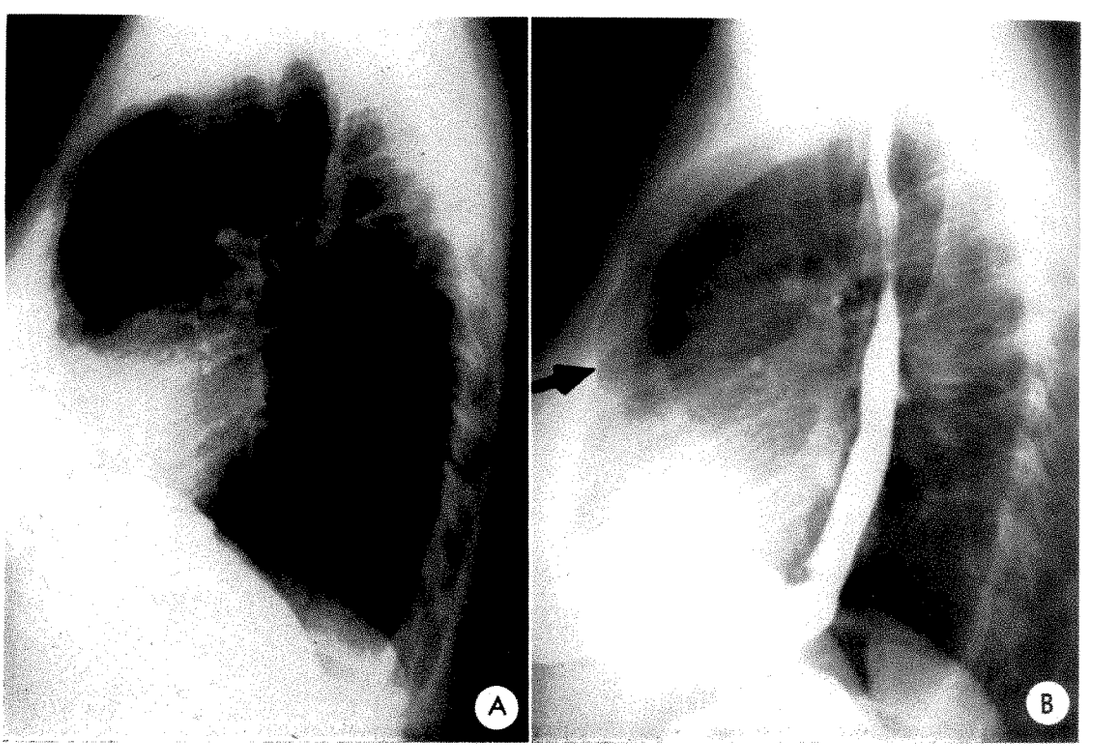




Fig. 6. Lateral roentgenogram showing sharp interface of the left lung with mediastinal fat (right arrowheads) at level of heart, but in the cephalic extension returning to the retrosternal area. The more anterior area of the left hemithorax appears blacker (left arrowheads) since more fat is seen on end interfaced with the soft tissue density of the heart.

MATERIAL AND METHOD

Adult and infant cadavers, which previously have been hanging in the upright position, were frozen in dry ice for 24 hours. They were then sectioned in the horizontal and sagittal planes on a bandsaw. Inflated lungs were also examined to evaluate their contours. Normal clinical roentgenograms, obtained in the frontal, lateral and oblique projections were studied. In addition, chest roentgenograms of 16 cases of proven thymomas were reviewed in the frontal and lateral projection, as well as other examples of various mediastinal masses and congenital abnormalities.

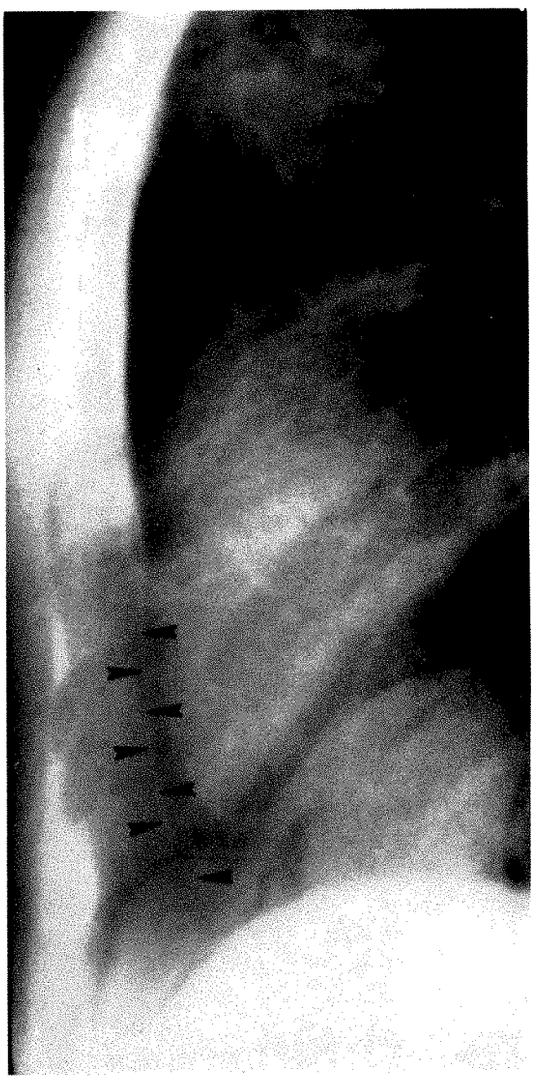


Fig. 7. Lateral chest roentgenogram showing a large amount of mediastinal fat outlining the pericardium (arrowheads). The anterior lobulated interface represents the superimposed anterior right lung.

RESULTS

Anatomically, in the normal adult, the right lung extends to the very anterior portion of the right hemithorax. In children, the superior portion of the right lung is excluded from the anterior chest wall by

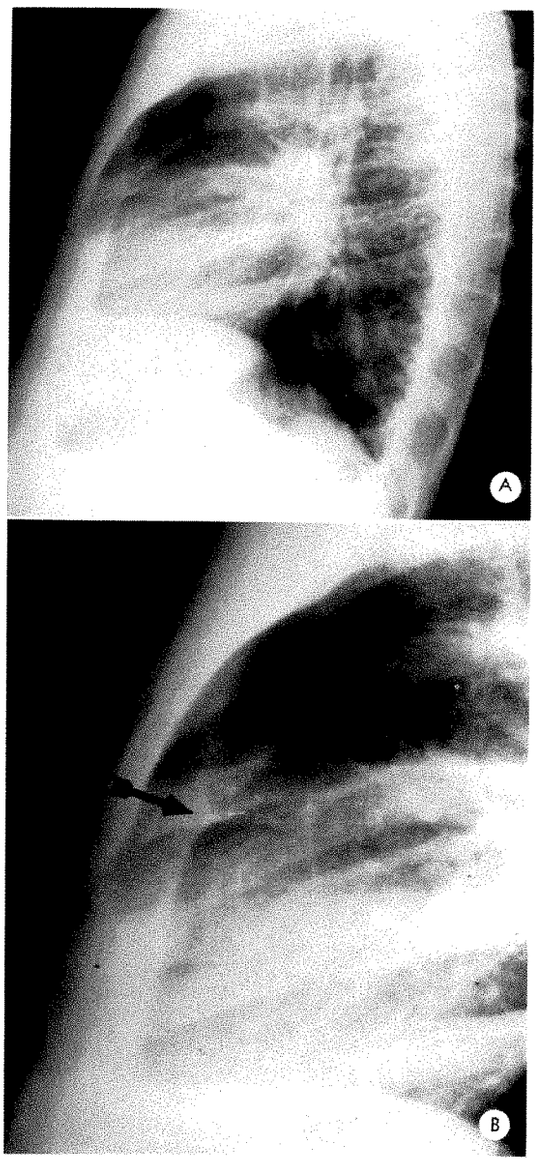


FIG. 8. (*A* and *B*) Oblique lateral chest roentgenograms, the right hemithorax projected posterior to the left, showing an apparent density caused by projected anterior surface of right lung (arrow). The anterior margin symmetrically follows the chest wall, excluding this as a retrosternal line.



FIG. 9. Lateral roentgenogram of the chest of a child, showing the anterior margin of the right and left lungs (arrowheads). The anterior margin of the left is more posterior at the level of the heart. Above the heart, the left lung maintains its retrosternal position. The cardiac incisura may thus be differentiated from merely an oblique roentgenogram.

Fig. 11. Summary diagram of the mechanism of shadows cast on a lateral roentgenogram. r = projected anterior surface of right lung; l = projected anterior surface of left lung; ↑ = projected mediastinal and pericardial fat.

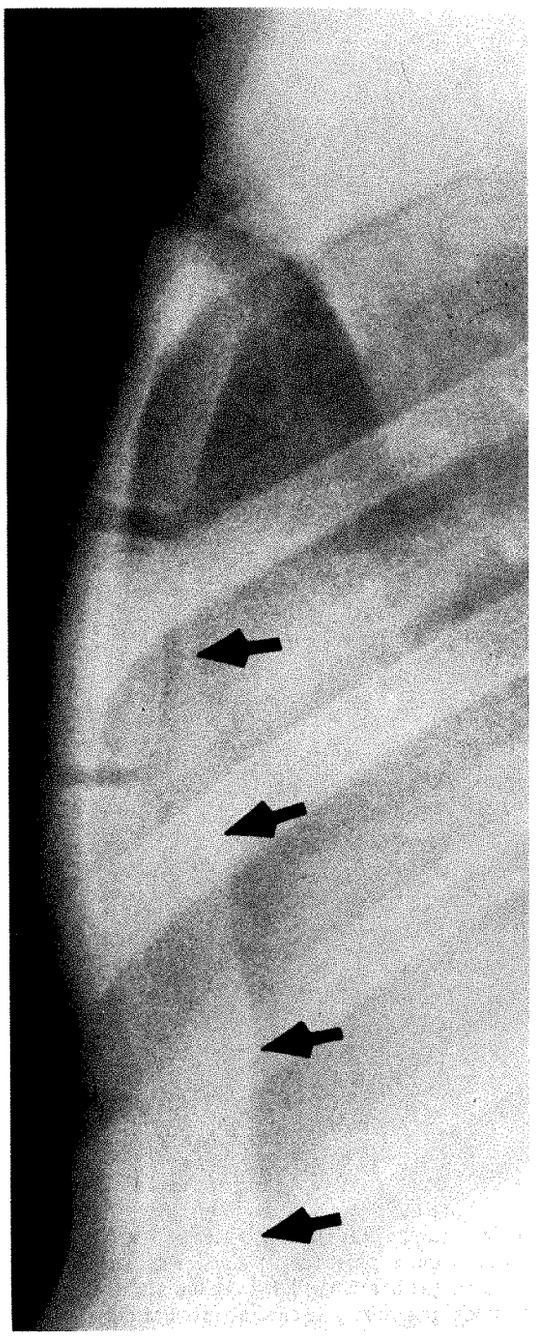


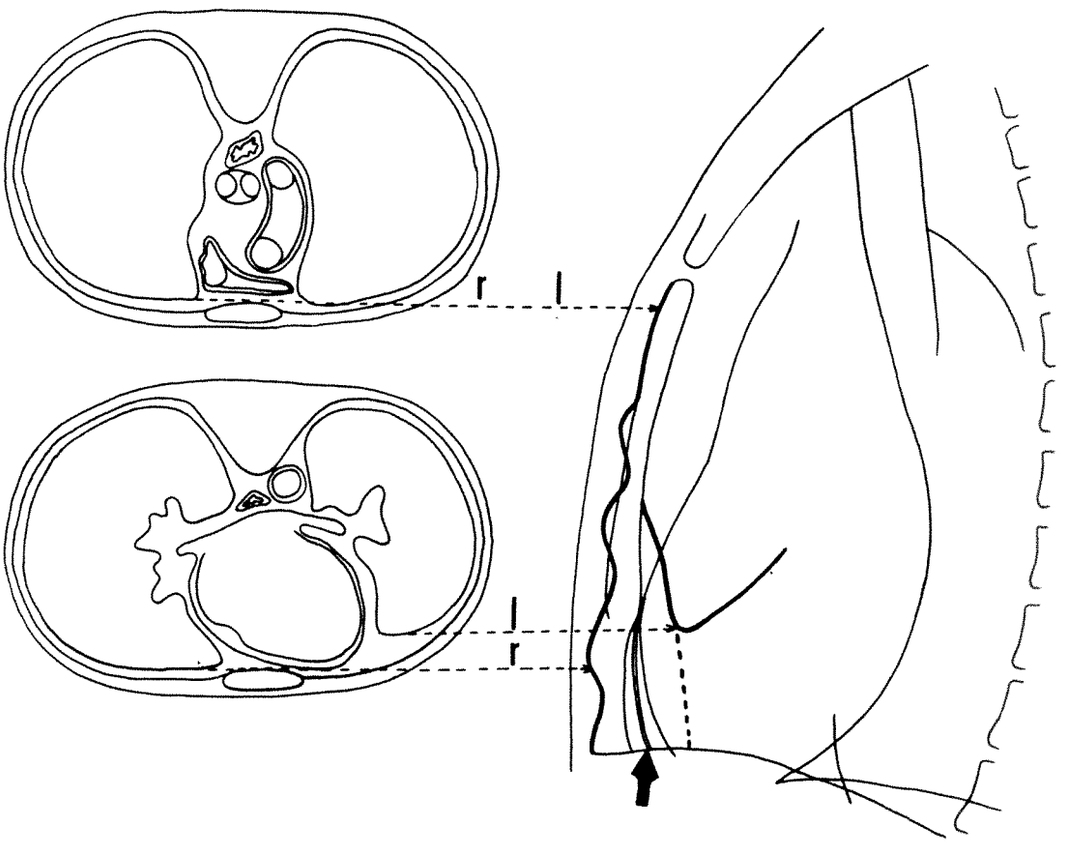
Fig. 10. Cardiac incisura in a child (arrows).

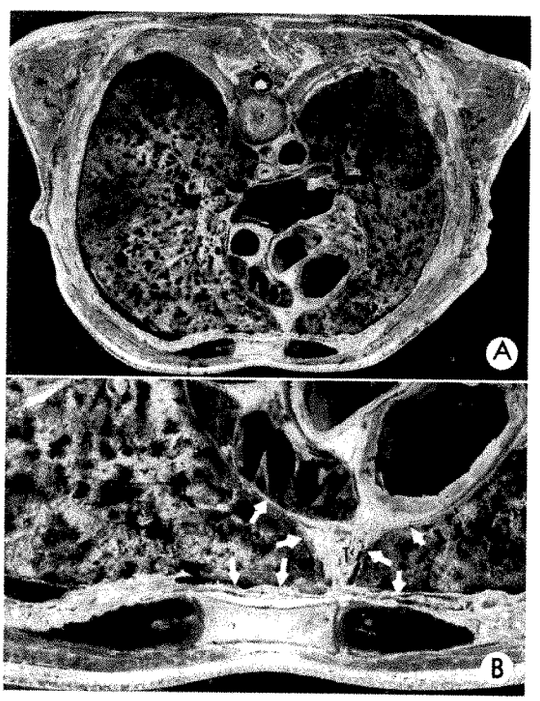
the normal thymus (Fig. 16). The left lung in the majority of cases is excluded from the anterior portion of the left hemithorax at the level of the heart, and, in children, superiorly at the level of the thymus (Fig. 1, *A–C*; 2, *A* and *B*; and 3, *A* and *B*).

A small percentage of specimens, however, had left lung anterior to the heart, separating it from the anterior chest wall. A varying amount of mediastinal fat was found anterior and to the left of the heart, at times interposing between the left lung and the chest wall (Fig. 1*A*).

The normal lateral roentgenogram showed variation in reflecting the anatomy described. Variation was accentuated by either changing the angle of the tube (Fig. 4, *A* and *B*) or the angle of the patient (Fig. 5, *A* and *B*; and 8, *A* and *B*). Shadows cast reflecting the normal anatomy, were occasionally lost by such angulations, presumably by taking away a significant interface of tissues of different densities to the roentgen beam (Fig. 11). The right lung was seen as a very anterior lucency having a lobulated contour corresponding to the shape of the anterior chest wall (Fig. 4, *A* and *B*; 5, *A* and *B*; 6; and 7). If the patient was slightly obliqued, projecting the right lung more posteriorly, a more lateral and posterior surface of the right was visualized. This surface, however, showed a contour paralleling the more anterior chest wall (Fig. 8, *A* and *B*). The anterior left lung showed variation. Occasionally, it may not be seen at all, or only after angulation of the tube or patient (Fig. 4, *A* and *B*; and 5, *A* and *B*). Above the level of the heart, when seen, it was immediately retrosternal in the adult. Lower, at the level of the heart, it was projected more posteriorly. It was most posterior at the maximal diameter of the heart.

The mediastinal fat varied in its appear





ance, at times not seen at all (Fig. 8, *A* and *B*), at times seen as a radiolucency (Fig. 4*B*; and 6), occasionally lucent enough to demonstrate the pericardium (Fig. 7), and at times seen as a relative opacity because of its contact with the more lucent aerated left lung (Fig. 5, *A* and *B*; 9; and 10).

Retrospectively, in a review of the roentgenograms of 16 cases of proven thymomas, 6 showed on random laterals, not specifically angled to bring them out, a retrosternal line, identified as the anterior surface of the lung on the side of the lesion

FIG. 12. (*A*) Anatomic cross section of the superior mediastinum. (*B*) Close-up of the retrosternal area showing the parietal pleural surface (arrows) separated from the sternum by fat and continuing around the heart and great vessels. This contains the thymus gland, T.

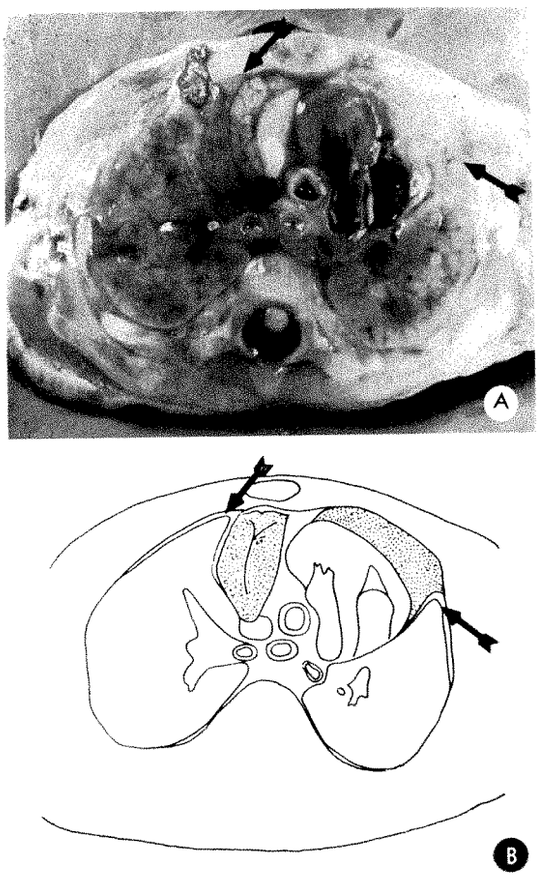


Fig. 13. (*A*) Cross section of the chest of newborn showing the lungs displaced (arrows). (*B*) Drawing of *A*.

(Fig. 14, *A* and *B*; and 15, *A–F*). Occasionally, other anterior mediastinal masses (such as ascending aortic aneurysms) were also seen to be associated with this line. Thymomas, however, arising anteriorly within the retrosternal space (Fig. 12, *A* and *B*; and 13, *A* and *B*) showed this most commonly.

Congenital abnormality with asymmetry of the thorax, the lungs and position of the heart may create this shadow (Fig. 17, *A* and *B*; and 18, *A* and *B*).

CONCLUSION

A shadow is appreciated on a roentgenogram because tissues of different radiodensities present a significant interface to

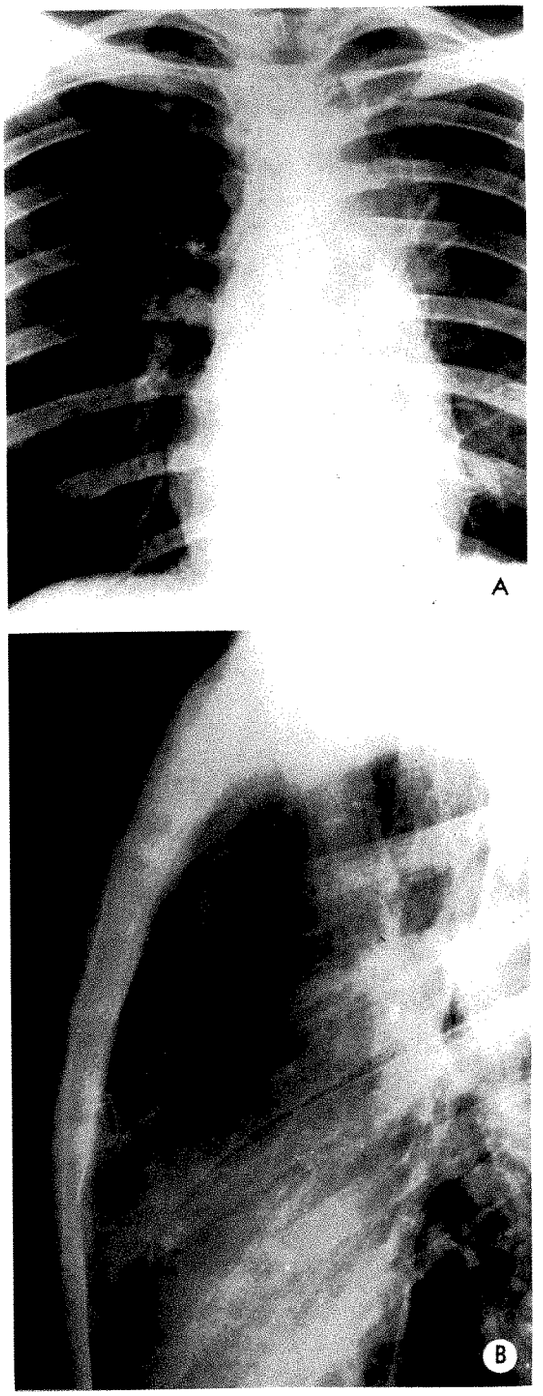


Fig. 14. Thymoma. (*A*) Anteroposterior roentgenogram showing mass in left upper hemithorax. (*B*) Lateral roentgenogram showing the retrosternal line, localizing it to the anterior mediastinum. The actual mass is not demonstrated. (Courtesy of Dr. E. Robert Heitzman, Syracuse, N. Y.)

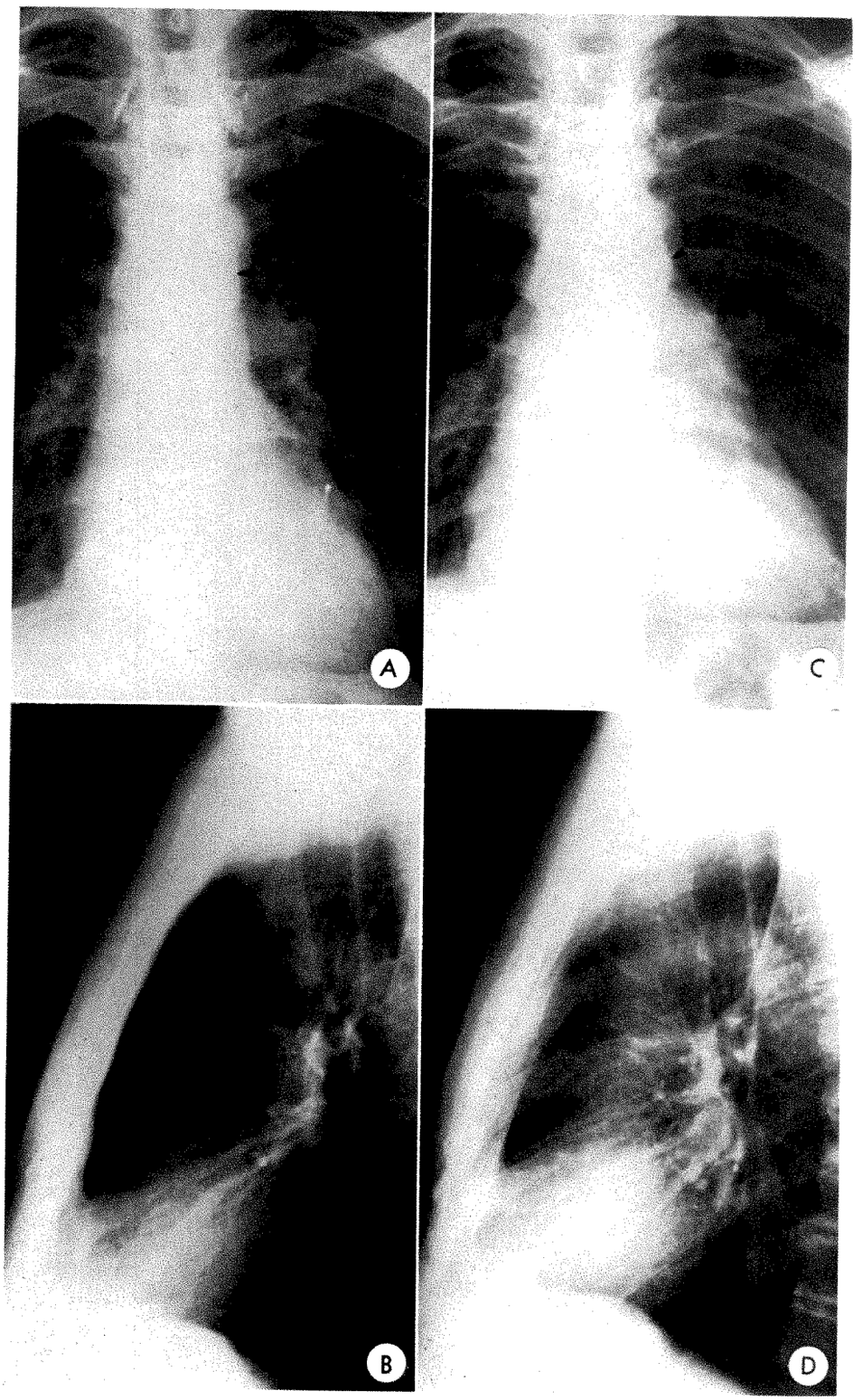


FIG. 15. (*A*) Posteroanterior roentgenogram showing minimal evidence of a mass (arrowhead). (*B*) Lateral roentgenogram which is normal. (*C*) Posteroanterior roentgenogram 2 years later showing definite mass. (*D*) Lateral roentgenogram showing retrosternal line (arrowheads). Mass definitely not seen, but localized at anterior mediastinum.

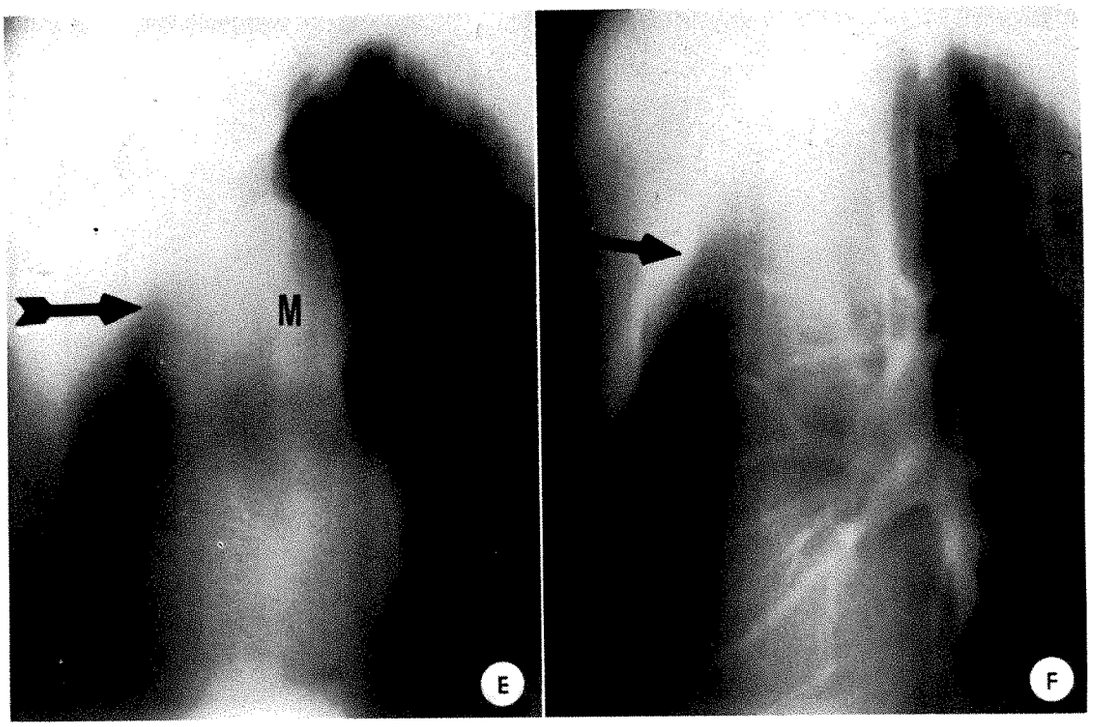


Fig. 15. (*E*) Lateral tomogram through the mass (M) showing the lung retracted (arrow). (*F*) Lateral tomogram to the right of the midline showing the right lung to be retrosternal (arrow).

the roentgen ray. The right lung consistently presents an interface which is anterior and uninterrupted, except superiorly in children because of the thymus gland. A retrosternal line is not commonly seen in children at this level, because of the soft nature of the thymus which displaces lung, but the lung maintains a tapering shape (Fig. 13, *A* and *B*) and merely blends with the density of the thymus gland. The normal thymus in children is then generally appreciated on the lateral roentgenogram as a relative density, not as a sharply demarcated mass. Its borders are seen in a posteroanterior or oblique projection, since a significant interface is presented between the lung and thymus.

The left lung is deficient at the level of the heart and, therefore, does not extend as anterior as the right lung. On many lateral roentgenograms with proper angulation, this may cast a shadow interfaced with the mediastinal fat. The deficiency of the left lung has been termed by anatomists "the cardiac incisura."[1] The mediastinal fat varies in amount, occasionally rich enough to cast a lucent shadow. Occasionally when interfaced with the aerated left lung it appears as a density.

No muscle indentation was detected on the anterior surface of the lungs of any specimens examined, caused by the transverse thoracic muscle to allow its visualization.[2]

Anterior mediastinal masses and particu-

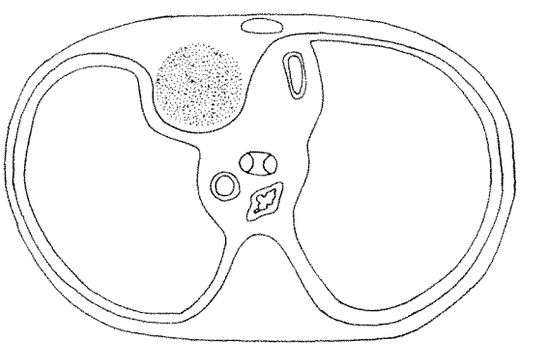


Fig. 16. Cross section diagram of thymoma showing the mechanism of the retraction of the lung and formation of the "thymic incisura" of the lung.

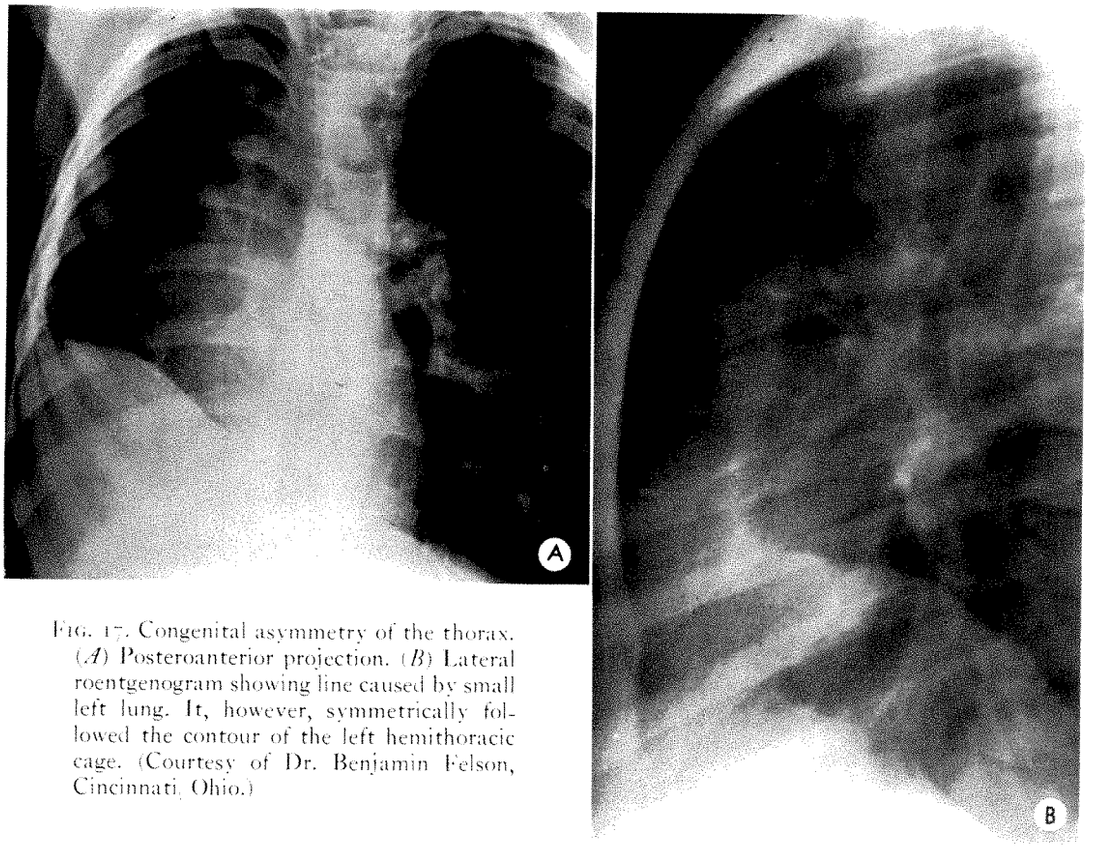


FIG. 17. Congenital asymmetry of the thorax. (*A*) Posteroanterior projection. (*B*) Lateral roentgenogram showing line caused by small left lung. It, however, symmetrically followed the contour of the left hemithoracic cage. (Courtesy of Dr. Benjamin Felson, Cincinnati, Ohio.)

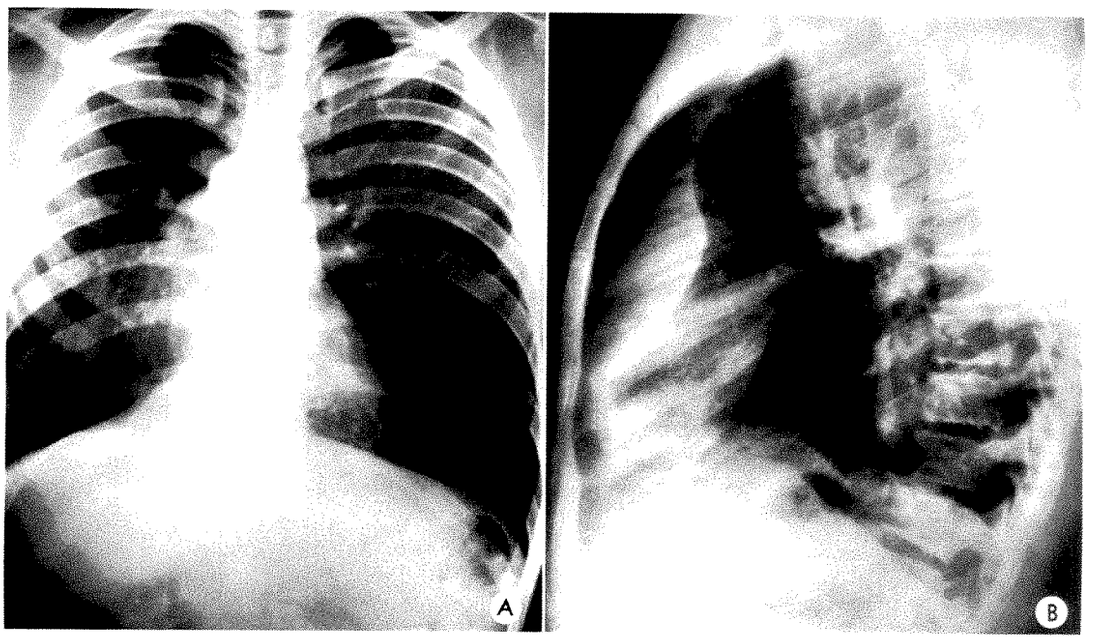


FIG. 18. Congenital anomaly. The heart is rotated and extends into the anterior portion of the right hemithorax. (*A*) Posteroanterior projection. (*B*) Lateral projection. The anterior surface of the right lung is outlined and an anomalous cardiac incisura is formed. (Courtesy of Dr. Benjamin Felson, Cincinnati, Ohio.)

larly thymomas, because of their site of origin, may be associated with a displaced lung casting a retrosternal line, analogous to the normal retrosternal line of the heart. This could be termed the thymic incisura. This then becomes a sign for the presence of an anterior mediastinal mass. If a mass is detected on other roentgenograms, the retrosternal line suggests its anterior location. Caution must be observed to exclude other causes for this shadow, such as congenital thoracic abnormalities and rotation of the lateral roentgenogram. The former should be apparent by correlation with the frontal roentgenogram, the latter by observing the shadow to be continuous all the way inferior, paralleling the projected anterior chest wall.

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ROENTGENOGRAPHIC FEATURES OF THYMOLIPOMA*

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THYMOLIPOMA is an uncommon benign tumor of the anterior mediastinum. Approximately 50 case reports[11] have been published, virtually all in the nonradiologic literature. In most of these reports the roentgenographic features of the tumor have not been emphasized or analyzed in detail. Although certain roentgenographic findings are often quite characteristic of thymolipoma, diagnosis prior to surgery or autopsy has been unusual.

A review of the roentgenographic findings discloses some distinctive and characteristic features that may often suggest the diagnosis.

REPORT OF A CASE

A 50 year old white woman, in good health until 6 months prior to her hospitalization, began experiencing recurring pain and swelling in the right calf. Phlebitis was diagnosed and treatment with anticoagulants was instituted. Subsequently, pain developed in the right foot, right ring finger tip and left forearm. Recurrent night sweats and fever also developed.

On hospital admission the patient appeared ill and had a temperature of 100° F. Physical examination disclosed slight splenomegaly, a Grade 2 to 4 systolic ejection murmur, petechial hemorrhages in the conjunctiva, calf tenderness and a tender finger pad. Biochemical and bacterial studies confirmed the clinical impression of subacute bacterial endocarditis; 6 consecutive blood cultures were positive for *Streptococcus viridans*.

Chest roentgenograms (Fig. 1, *A–C*) were interpreted as pericardial and possibly pleural effusion.

While under treatment with high doses of penicillin, signs of aortic insufficiency developed, suggesting rupture of an aortic leaflet. Progressive cardiac failure could not be controlled, and the patient died 64 days after admission.

At autopsy the heart was moderately enlarged, showing evidence of verrucous endocarditis of the aortic valve and a perforation of a valve leaflet.

Between the lungs and the diaphragm there was a multilobular mass of fat yellowish-gray tissue, extending in the anterior mediastinum, anteriorly to the pericardium. This mass was entirely intrathoracic and caused an upward displacement of both lungs. The entire mass weighed 2,400 gm. This mass was covered by pleura; it was intrapleural bilaterally and was located anteriorly. It was very easily separated from the lungs and showed a multilobular appearance. The cut surface demonstrated yellowish-grayish tissue which in some areas was hemorrhagic (Fig. 2, *A* and *B*).

Histologically, the tumor revealed extensive areas of a mature adult type of adipose tissue interspersed with islands of residual thymic tissue with characteristic Hassall's corpuscles and small thymocytes. Delicate strands of fibrous connective tissue separated the adipose tissue in irregular lobules. A thin but well defined capsule was identified (Fig. 2*C*). Pathologic diagnosis: thymolipoma; subacute bacterial endocarditis.

DISCUSSION

Thymolipoma comprises 2–9 per cent of thymic tumors.[9,11] Mediastinal lipomas of nonthymic origin are somewhat more common.[11] The earliest description of thymolipoma was by Lange in 1916; subsequently about 50 case reports have been published. The tumor has no sex predilection, and can occur at any age. The youngest patient was 4 years of age, the oldest 54 years; the average age at time of discovery was 22 years.[8]

The tumor originates in the anterior

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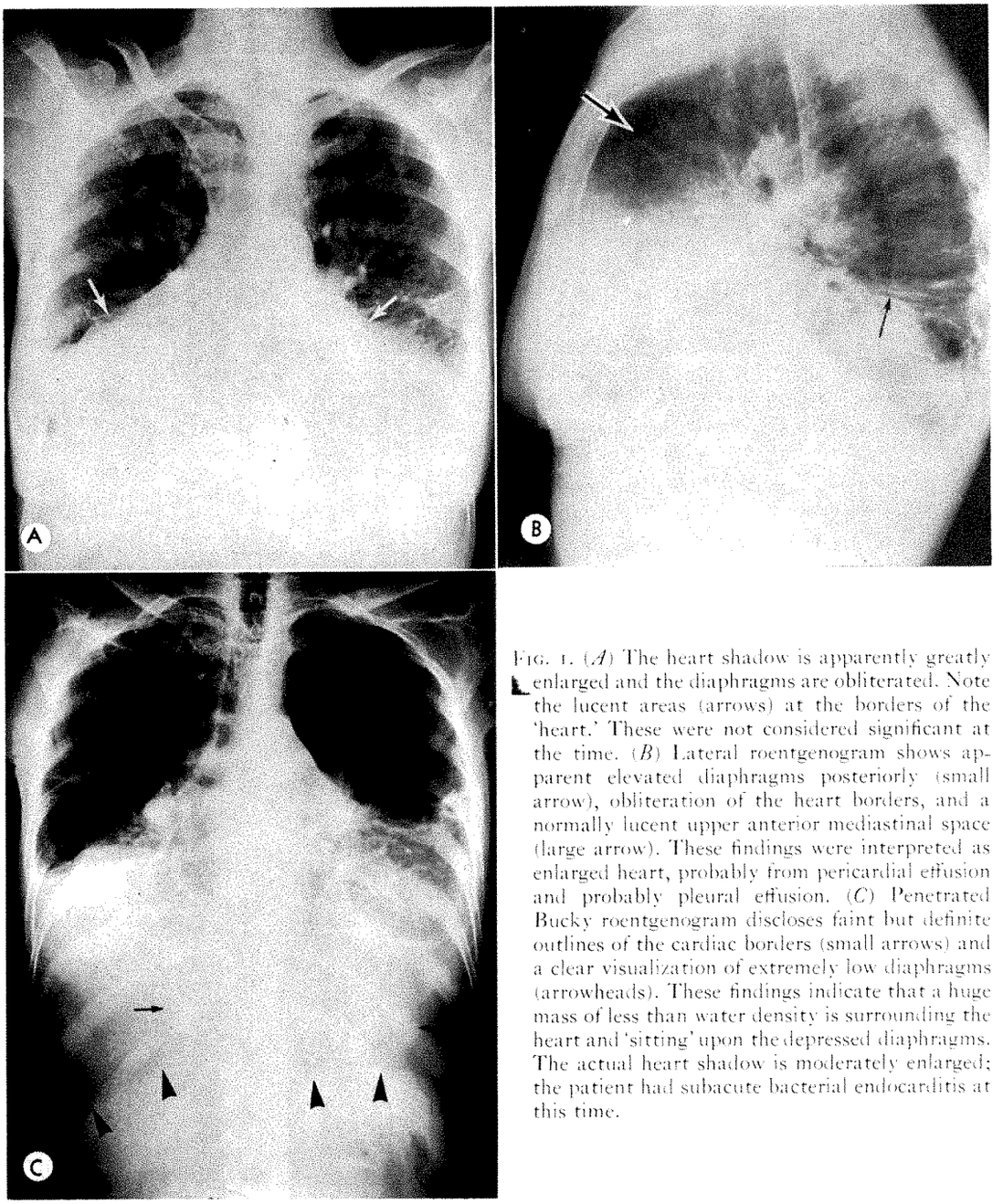


FIG. 1. (*A*) The heart shadow is apparently greatly enlarged and the diaphragms are obliterated. Note the lucent areas (arrows) at the borders of the 'heart.' These were not considered significant at the time. (*B*) Lateral roentgenogram shows apparent elevated diaphragms posteriorly (small arrow), obliteration of the heart borders, and a normally lucent upper anterior mediastinal space (large arrow). These findings were interpreted as enlarged heart, probably from pericardial effusion and probably pleural effusion. (*C*) Penetrated Bucky roentgenogram discloses faint but definite outlines of the cardiac borders (small arrows) and a clear visualization of extremely low diaphragms (arrowheads). These findings indicate that a huge mass of less than water density is surrounding the heart and 'sitting' upon the depressed diaphragms. The actual heart shadow is moderately enlarged; the patient had subacute bacterial endocarditis at this time.

mediastinum, and is attached to the base of the heart by a vascular pedicle. Grossly, the tumor is always yellowish, soft and pliable; often it is lobate with thin edges. It can attain huge proportions: 68 per cent were over 500 gm.; 23 per cent over 2,000 gm., and 1 tumor weighed over 12,000 gm.[11] In our patient, the tumor weighed 2,400 gm.

Since the tumor is soft and pliable, the larger thymolipomas slump onto the diaphragms and adapt themselves to the diaphragmatic contours, thus becoming largely an inferior anterior mediastinal lesion. His-

tologically, all the tumors consist of adult adipose tissue interspersed with areas of normal, hyperplastic or atrophic thymic tissue.

The thymolipoma causes few or no symptoms, even when quite large. In some patients there were episodes of cough and dyspnea, but chest pain was exceedingly rare.[1] Neither myasthenia gravis nor any other syndrome is associated with thymolipoma. Fortuitous association of the tumor with other conditions, of course, can occur, such as endocarditis in the above reported case, or Graves' disease in Trites' patient.[13] In fact, almost all thymolipomas were incidental discoveries on chest roentgenograms made routinely or for an unrelated illness. The average interval between diagnosis and removal was 4 years, attesting to the lack of symptoms.

ROENTGENOGRAPHIC FEATURES

The thymolipoma apparently originates in the atrophic thymus, and, when still small, appears as a sharply circumscribed round or oval mediastinal density, anterior to the base of the heart.[1] Its roentgenographic density is less than that of a nonfatty mass, but this may be difficult to appreciate when the tumor is entirely surrounded by air-bearing tissue. As the tumor enlarges, it almost extends caudad, probably due to gravity, and the moderately large lesion appears as a circumscribed density, overlying one or both sides of the heart in the frontal view.[14-18] Calcification has never been reported. The tumor does not cause pleural effusion.

The large thymolipomas, which constitute the majority of the reported tumors,[11] produce the more interesting roentgenographic findings. As the soft, pliable mass enlarges, it molds and accommodates itself to the potential spaces between the lungs and the heart, diaphragms, or anterior mediastinum. It becomes an anterior inferior mediastinal mass, but produces little or no compromise of respiratory or cardiac activity; it causes no significant cardiac displacement. Because of this accommoda-

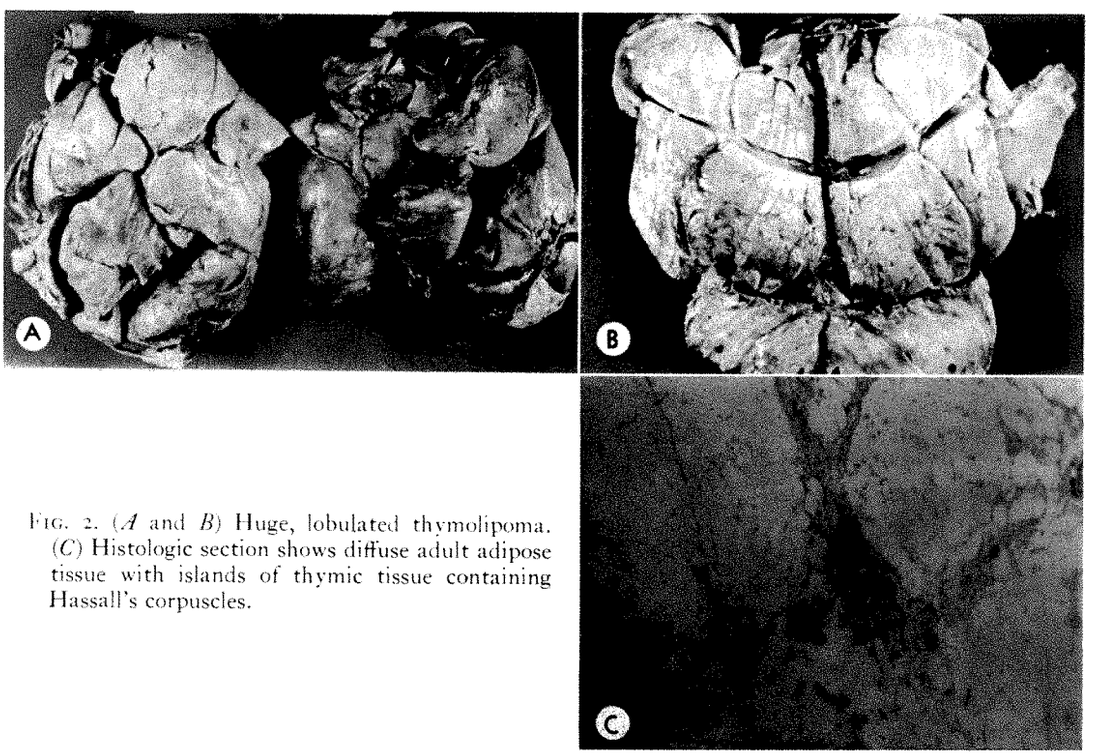


FIG. 2. (*A* and *B*) Huge, lobulated thymolipoma. (*C*) Histologic section shows diffuse adult adipose tissue with islands of thymic tissue containing Hassall's corpuscles.

tion and the absence of symptoms, the thymolipoma, although slow growing, is frequently quite large at the time of discovery. Moigneteau and Cornet[11] indicate that this large fatty mass will show changes in shape on postural roentgenograms, which may be a clue to its plastic character. This large anterior inferior mediastinal density often simulates an enlarged heart shadow (Fig. 1*A*) in the frontal view. In the lateral view, the tumor mass overlies the heart shadow; larger tumors extend posteriorly between the lung and the diaphragm, simulating elevation of one or both diaphragms (Fig. 1*B*). The lucent upper anterior mediastinal space may be unaffected, which is quite unusual in other sizeable anterior mediastinal masses. Unexplained cardiac enlargement was the original roentgenographic impression in many of the larger thymolipomas.[1,5,7,8,10–14] However, a normal position of the barium filled esophagus on the lateral roentgenogram is strong evidence against cardiomegaly.

In many of the cases, angiocardiography was utilized[1,8,12,13] to determine the nature of the puzzling and sometimes bizarre appearing 'cardiac enlargement.' In a review of 24 case reports, Benton and Gerard[1] observed that angiocardiography had been done in 7 patients to rule out cardiac enlargement. When a large thymolipoma extends unilaterally, one side of the heart shadow is obscured and the appearance may simulate a large pleural tumor[3] or, in 1 case, a basal atelectasis.[4] Diagnostic pneumomediastinum will show the mass to be distinct from the heart and lungs.[4,11]

However, we believe that the density can be identified as a large anterior mediastinal fatty mass from the plain chest roentgenograms, if the difference in density between the more lucent fatty mass and contiguous water-density structures is observed and evaluated. In addition, the thin periphery of a thymolipoma often appears considerably more lucent than its thicker central portion,[11,12] and the lucent edges (Fig. 1*A*) should suggest that these are *not* the borders of an enlarged heart. More significant findings, however, will be seen on a well penetrated Bucky roentgenogram (Fig. 1*C*). The tumor, lying directly over the heart and diaphragms, will obscure these structures on conventionally exposed chest roentgenograms, but on properly penetrated films, the decreased roentgenographic density of the fatty mass will allow recognition of the true underlying cardiac borders and the diaphragmatic shadows. This significant and virtually diagnostic finding is strikingly illustrated in our patient. The conventional roentgenograms (Fig. 1, *A* and *B*) revealed an apparently enlarged cardiac shadow and elevated diaphragms. On the penetrated Bucky roentgenogram (Fig. 1*C*) faint but definite heart borders are perceived and the actual diaphragmatic shadows, considerably depressed by the huge mass, are visualized. Such findings can only occur if a large fatty mass is surrounding the heart and is in contact with the diaphragms. Similar findings were also observed by Trites,[13] and by Rubin and Mishkin[12] on penetrated roentgenograms made during angiography. Benton and Gerard,[1] and Moigneteau and Cornet[11] also have noted the decreased density of the thymolipoma. In the majority of the other reported cases, however, either well penetrated roentgenograms were not made or the fatty density on such roentgenograms was not appreciated; roentgenologic diagnosis of a mediastinal lipoma or thymolipoma was exceedingly rare.[3,8,13]

The roentgenographic differential diagnosis of the smaller thymolipoma includes thymic cyst, thymoma, teratoma and nonthymic mediastinal lipoma. The large thymolipoma must also be distinguished from cardiac enlargement, pericardial effusion, pericardial cyst or tumor and atelectasis of a lobe. Angiocardiography or pneumomediastinum will eliminate these latter possibilities. If the fatty density is appreciated roentgenographically, only a simple lipoma and liposarcoma may have to be considered. The former rarely becomes as large as a thymolipoma; the latter usually causes severe chest symptoms, signs of

mediastinal compression and frequently pleural effusion.[2,12,15]

CONCLUSION AND SUMMARY

1. The thymolipoma usually begins in young individuals and, being virtually asymptomatic, may attain huge proportions before discovery.

2. The smaller lesions cannot be distinguished roentgenographically from other benign anterior mediastinal masses.

3. The large tumors tend to slump toward the diaphragms, leaving the anterior superior mediastinal space lucent, an unusual finding in the majority of large mediastinal tumors. Often the large mass simulates cardiomegaly, but a normal position of the esophagus on the lateral roentgenogram is evidence against significant cardiac enlargement.

4. Well penetrated chest roentgenograms will usually demonstrate the outlines of the underlying heart and diaphragms, since these structures are always of greater roentgenographic density than the fatty tumor. This finding is virtually pathognomonic and will obviate the need for angiocardiography or pneumomediastinum.

5. The thin periphery of the tumor may be considerably more lucent than the bulky center—a suggestive finding.

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THERMOGRAPHY AND VENOGRAPHY IN TUMORS OF THE MEDIASTINUM AND CHEST*

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COMPLETE or partial obstruction of the superior vena cava or the innominate veins may be responsible for varying degrees of facial edema, dyspnea, prominent venous distention, and cerebral edema. Whether this represents an immediate radiotherapeutic emergency is questionable, but these patients become more comfortable as radiation therapy proceeds. Early, severe symptoms may be related to absence of venous collaterals, which, as they become functional, will also relieve symptoms.

Superior venacavography, therefore, is not important in the establishment of the diagnosis of venous obstruction in tumors of the chest and mediastinum, but rather in the localization of the obstruction, so that localized radiation therapy may be effectively administered.

MATERIAL AND METHOD

Percutaneous antecubital vein puncture was performed bilaterally in 15 patients with mediastinal or pulmonary tumors. A test dose of 10 cc. of 60 per cent meglumine diatrizoate was injected on each side and the contrast material flow was observed fluoroscopically. If the flow was unimpeded, 40 cc. of contrast material was injected into the vein on each side in 3 to 4 seconds, and films were exposed with a film changer at a rate of 1 film per second for 10 seconds. If jugular reflux or venous obstruction was observed fluoroscopically, the quantity of contrast material was reduced to 20 cc. on the involved side during the filming sequence.

These same 15 patients were then studied

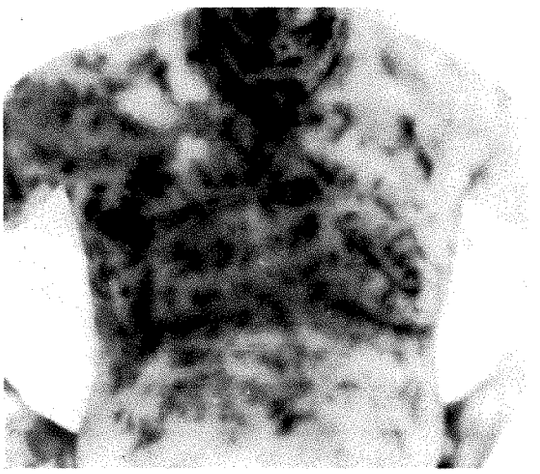


FIG. 1. This patient was under treatment for squamous cell carcinoma of the lung. Venography demonstrated normal appearing innominate veins and a normal superior vena cava. This thermogram demonstrates an irregular heat pattern over the scanned area.

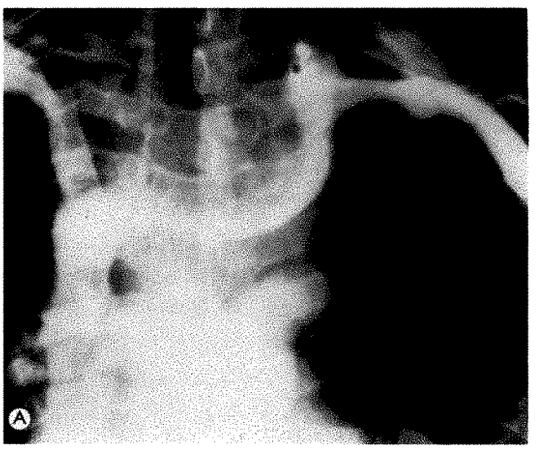


FIG. 2. (*A*) The venogram in this patient demonstrates inferior displacement and compression of the left innominate vein.

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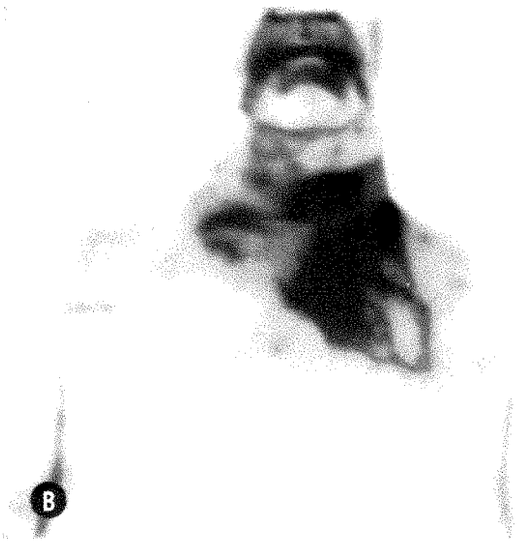


FIG. 2. (*B*) The thermogram demonstrates the unilaterality of the abnormality, and there is probably some contribution from the primary tumor as well.

with a high resolution Texas Instrument ThermIscope which has a mercury cadmium telluride detector. The spectral range of the detector is 6 to 14 micrometers, which corresponds closely with the emissivity of the skin. The scanning mechanism and associated optics selectively focus the emitted radiation from the patient on the detector. The electrical signal generated in the detector is processed by the electronics which relate surface temperature of the patient to a visual image on a high resolution cathode ray tube. The thermographic image is displayed electronically and viewed directly, and can be recorded on Polaroid type P/N 55 film.

The patients were positioned at focal distances between 50 and 65 cm. depending upon the area of interest. Room temperature was maintained at 21° C., and patients cool adapted for at least 10 minutes prior

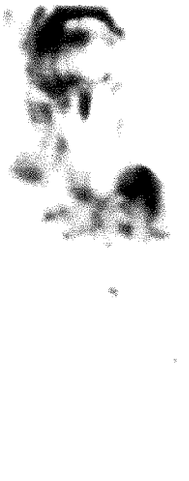


FIG. 3. (*B*) The thermogram confirms the unilaterality of the occlusion, with an increased heat pattern over the left upper thorax.

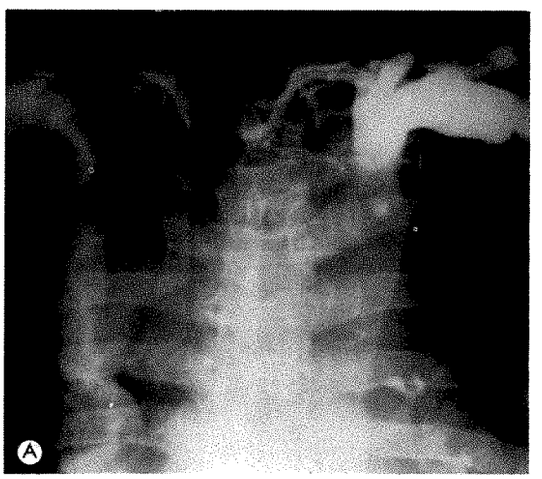


FIG. 3. (*A*) Venography demonstrates complete occlusion of the left innominate vein, with collateralization to the right innominate vein and reflux into the left jugular vein.

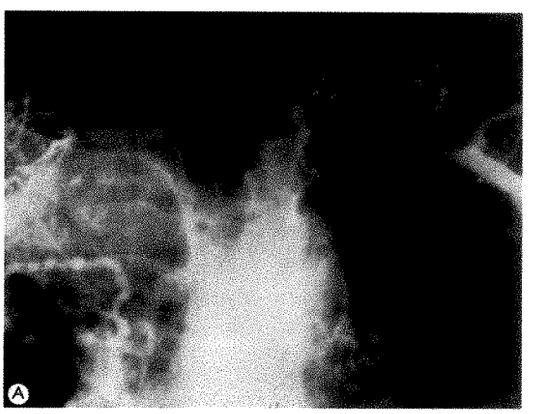


FIG. 4. (*A*) The innominate veins and the superior vena cava do not opacify; extensive venous collateralization is evident in the upper thorax and neck.



Fig. 4. (*B*) The thermogram demonstrates the extent of the collateralization with a vertical area of increased temperature approximately 15 cm. wide extending from the neck to the abdomen. Multiple lateral chest wall veins and abdominal veins are clearly visualized.

to the scan. The temperature and sensitivity settings on the ThermIscope were individually adjusted for each patient, but a temperature setting of 31° C. and a sensitivity range of 6° C. were usually employed.

RESULTS

Two patients had normal venous angiograms. One had a homogeneously irregular thermographic pattern over the entire area that was scanned (Fig. 1). The thermogram in the other patient was normal.

Thirteen patients had abnormal venograms. Ten of these had innominate vein involvement by tumor, either unilateral or bilateral, and the remaining 3 patients had tumor compromising and compressing the superior vena cava (Fig. 2*A*; and 3*A*). The unilaterality of the lesion could be predicted on the basis of the thermogram (Fig. 2*B*), and even though collateral vessels were present (Fig. 3*B*), the venogram and thermogram correlated unilaterally except in 2 patients. In both of these patients, innominate vein abnormality was present bilaterally angiographically, which correlated with bilateral thermographic abnormality, but the thermograms were more markedly abnormal on the right, the apex of the right lung being the site of primary tumor in both patients. Obvious total caval obstruction angiographically (Fig. 4*A*) correlated with the thermogram (Fig. 4*B*).

The correlation between angiograms and thermograms was good in 14 patients, 1 of whom had normal studies. The other patient (Fig. 1) had a normal angiographic study and a bizarre thermogram, unrelated to local venous compromise.

DISCUSSION

Venous studies of the innominate veins and superior vena cava employing positive contrast medium are useful to localize tumor extension and to more effectively outline radiation therapy portals.

Thermography correlates with venography, but less effectively localizes tumor extent.

Thermography is a rapid examination with no patient morbidity, while angiography has some associated potential morbidity.

SUMMARY

Screening thermography in patients with lung or mediastinal tumor selects those patients with more extensive tumors involving the major veins of the upper thorax.

The patients thus selected should have roentgenographic studies of these veins to effectively outline the required larger radiation treatment portals.

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ACUTE MEDIASTINAL WIDENING*

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ACUTE widening of the mediastinum is an infrequently observed roentgenologic finding which may be due to sudden development or increase in size of a mass lesion, particularly lymphadenopathy, or the sudden accumulation of fluid material in the mediastinum.

In this paper only the latter group is considered, since lymphadenopathy and other mass lesions usually demonstrate the characteristics of a localized mass and can be distinguished from diffuse mediastinal engorgement.

MATERIAL

Blood, pus, chyle and edema fluid all may cause acute mediastinal enlargement. Rupture of a viscus or vessel passing through the mediastinum is the most common cause of acute mediastinal widening, but occasionally edema fluid or purulent material will collect without such a predisposing factor. Most of the roentgenographic findings are nonspecific; however, correlation with the clinical course will often allow a specific diagnosis.

Differentiation from chronic mediastinal widening may be impossible without previous roentgenograms for comparison, since tortuous vessels, neoplastic and fibrous tissue may cause widening of the mediastinum indistinguishable from an acute process. Clinical findings or a pleural effusion may help in this determination, as mediastinal fluid frequently escapes into the pleural space or is associated with concomitant pleural disease.

MEDIASTINAL HEMORRHAGE

Mediastinal hemorrhage is occasionally spontaneous, but usually is seen after trauma. Blunt trauma usually results in venous bleeding and associated fractures are often visible roentgenographically. Occasionally blunt trauma causes rupture of a great artery in which case hemorrhage is usually catastrophic.[13] Perforating trauma may involve arteries or veins and has been associated with many medical procedures, including placement of a central venous pressure catheter, sternal bone marrow aspiration, pericardiocentesis, intracardiac injections, arteriography,[6] cardiac catheterization, and cervical or thoracic surgery.

Spontaneous mediastinal hemorrhage has been described in a wide variety of conditions, including various coagulopathies, uremia,[4] and neoplastic disease.[5] Aortic dissection and leakage is probably the most common cause of spontaneous mediastinal bleeding. This diagnosis is confirmed by aortography. We have even seen a case of massive spontaneous hemorrhage with no discernible predisposing cause at surgery or on clinical follow-up (Fig. 1).

The diagnosis of hemorrhage may be difficult to make without a history of appropriate trauma or demonstrable aortic disease. Experimental cadaver work by Raphael[20] showed that the usual roentgenographic appearance is lobulated expansion on the left side of the mediastinum, because strong fibrous attachment of the mediastinum to the pericardium prevents accumulation on the right. We have not found this to be a reliable or helpful observation clinically.

MEDIASTINAL PUS

Acute suppurative diseases of the mediastinum may be localized or diffuse. Mediastinal pus results from a variety of conditions especially perforation of a viscus and extension from adjacent areas.

Esophageal perforation is either spontaneous or secondary to instrumentation,

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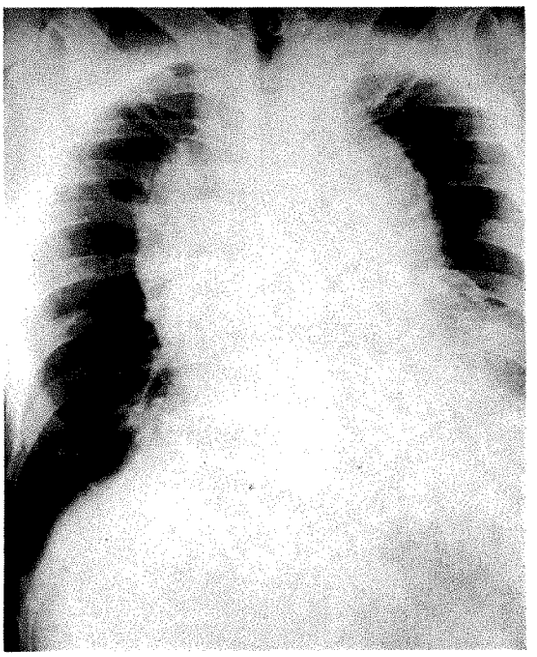


FIG. 1. Posteroanterior chest roentgenogram of a patient with spontaneous mediastinal hemorrhage of unknown etiology shows massive, diffuse mediastinal enlargement.

leakage at the site of surgical anastomosis, erosion from a primary carcinoma or an impacted foreign body. Rupture of the esophagus is the most serious and rapidly fatal perforation of the gastrointestinal tract, and mediastinal widening from this cause often must be diagnosed by the radiologist to avoid a fatal outcome. When due to instrumentation, perforation is usually at the esophageal inlet or a biopsy site. Spontaneous perforation (Boerhaave's syndrome) almost always involves the lower esophagus just above the diaphragm along its left lateral aspect and usually is associated with a history of antecedent vomiting.[1] Mediastinal emphysema is an early and valuable sign of esophageal rupture. In spontaneous perforation it often appears initially only as a thin radiolucent line behind the heart. Subcutaneous emphysema in the neck may be seen later. With spillage of esophageal and gastric contents there is rapid progression of suppurative mediastinitis which is manifested by diffuse mediastinal widening and loss of the sharp interface between the mediastinum and the adjacent lung. Extension into the pleural space is common and results in pyothorax or pyopneumothorax, more often on the left. The diagnosis is best confirmed by demonstration of the site of rupture with contrast media (Fig. 2, *A* and *B*).

Rupture of the tracheobronchial tree with associated acute mediastinitis is almost invariably post-traumatic and is usually associated with pneumomediastinum and air in the tissue planes of the neck.[7] Associated fractures of the superior ribs, frequently of the first 3, are often seen with traumatic rupture of the tracheobronchial tree and provide a valuable roentgenographic clue to its presence.[8]

Abscesses may be found anywhere in the mediastinum, and their location often gives a clue to the etiology. Those which contain air as well as fluid are secondary to rupture of a hollow viscus or infection with gas forming organisms, particularly in diabetics.[14] In addition to the local mass produced by the abscess, there is often a generalized widening of the mediastinum due to diffuse inflammatory reaction.[12] Abscesses in the posterior mediastinum are usually secondary to tuberculosis or pyogenic infections of the spine. Such lesions seldom give rise to mediastinal symptoms.[12] Detailed roentgenograms of the dorsal spine usually show the osseous or disk space involvement. Superior mediastinal abscesses are often extensions of neck abscesses. In children the initial site of infection is usually the retropharyngeal space whose fascial planes are in direct communication with the mediastinum. In these cases the trachea is often deviated anteriorly[11] with an associated soft tissue density extending to the right.[7] The abscess may burrow through the pleura into the adjacent right upper lobe.[17] Swelling in the neck and a recent history of pharyngitis are helpful clinical findings. A lateral roentgenogram of the neck may show widening of the retropharyngeal soft tissue space. Abscesses in the anterior mediastinum are rare and most commonly follow penetrat-

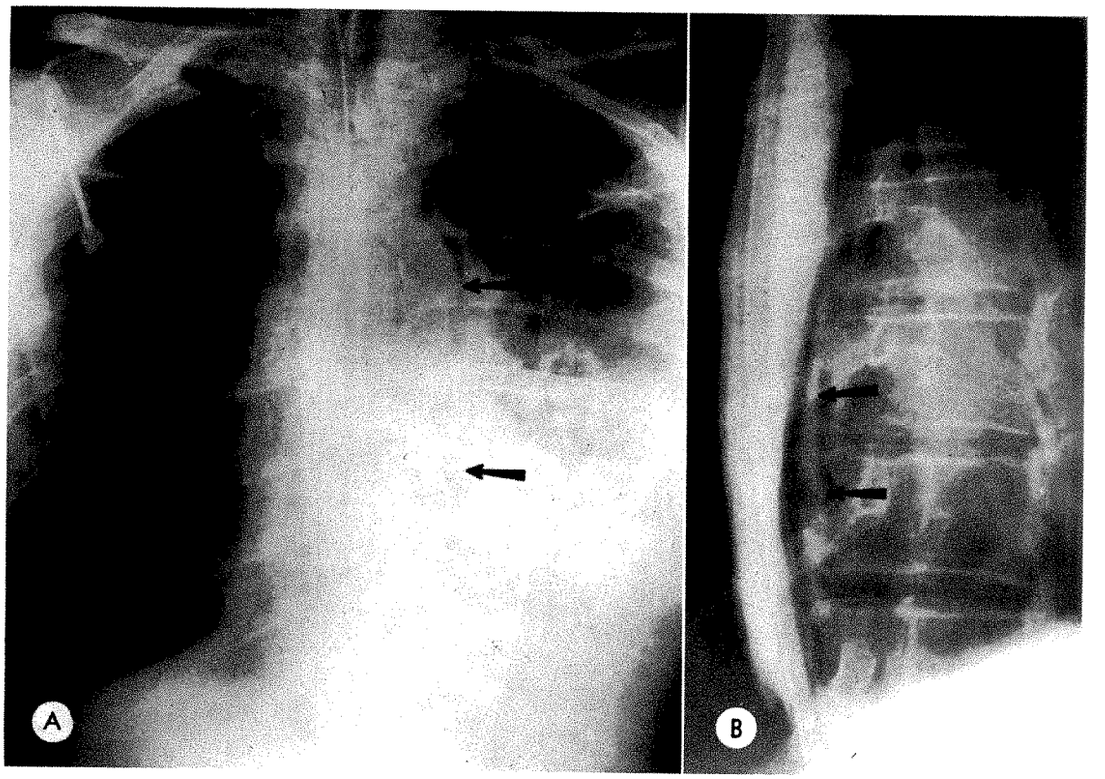


FIG. 2. (*A*) Posteroanterior chest roentgenogram of a patient with spontaneous perforation of the esophagus shows a left pleural effusion, mediastinal widening with blurred margins, and pneumomediastinum (arrows). (*B*) The esophagogram shows extravasation of the contrast medium (arrows).

ing wounds of the anterior thorax.[2]

Pancreatitis may also involve the mediastinum, presumably extending through the aortic and esophageal hiatuses.[18] We have not observed acute mediastinal widening from this source, but we have seen several pancreatic pseudocysts in this location and presumably roentgenograms during the acute episode would reveal the development of widening.

MEDIASTINAL CHYLE

Mediastinal widening may occur as a result of the accumulation of chyle in the posterior mediastinum. Chylomediastinum and chylothorax have been associated with thoracic duct pathology secondary to trauma (surgical and nonsurgical),[15,21] malignancy,[16] congenital malformations, infection and idiopathic conditions.[19,22] Rapid development of a large left-sided pleural effusion after surgery involving the mediastinum without an associated drop in hematocrit is highly suggestive of a ruptured thoracic duct.

The thoracic duct originates from the cisterna chyli in the retroperitoneum anterior to the body of the second lumbar vertebra. It ascends into the posterior mediastinum through the aortic hiatus remaining between the aorta and azygous vein up to the level of the fifth thoracic vertebra, where it passes to the left behind the aorta and empties into the venous system at the junction of the left subclavian and internal jugular veins.[9]

Mediastinal widening is often not prominent when chyle escapes from the thoracic duct but chylothorax usually results. As might be expected from the course of the duct, leakage in the inferior portion is usually into the right pleural space and more superior leaks go into the left pleural space. Higgins and Mulder[10] reported 4

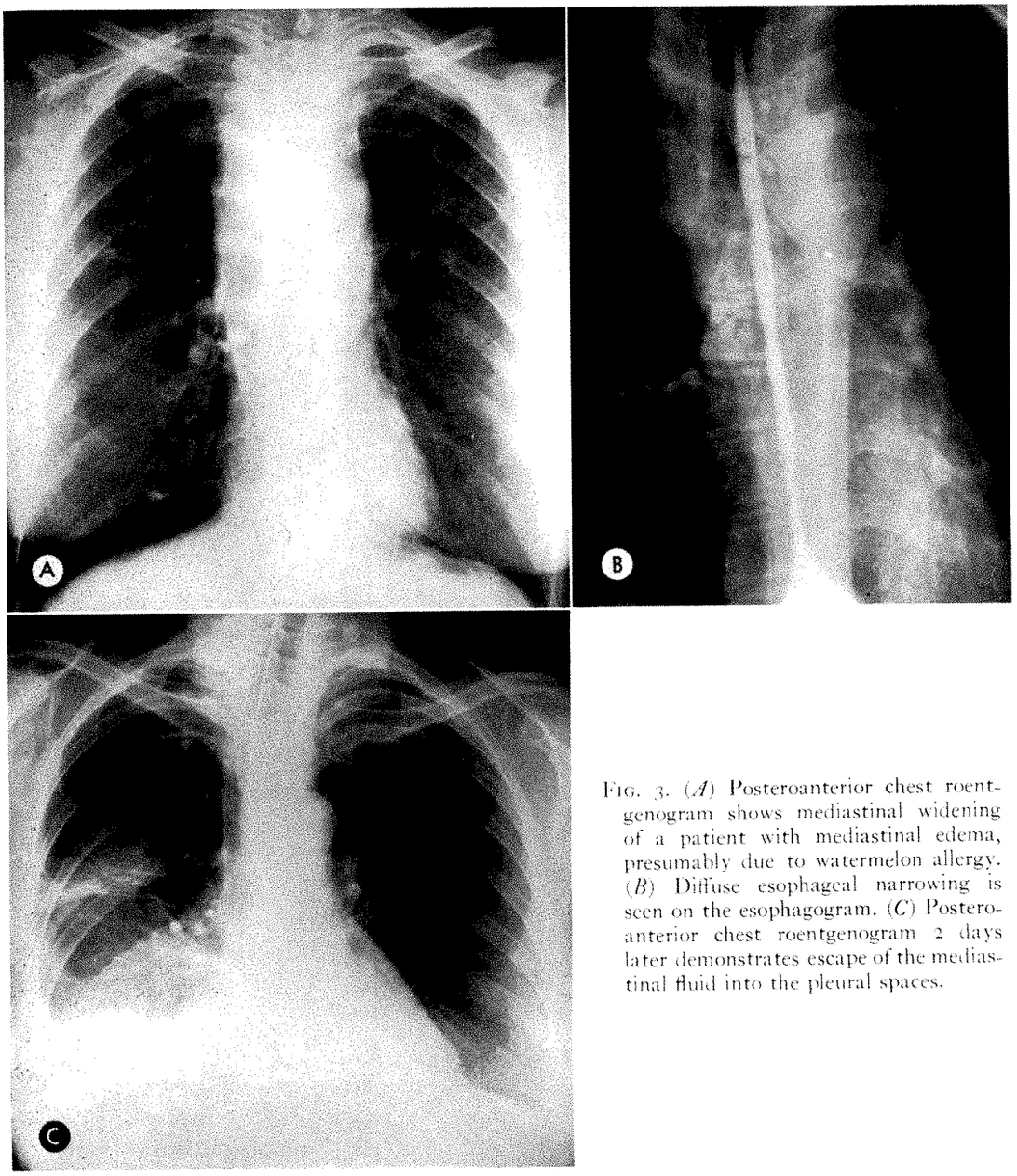


FIG. 3. (*A*) Posteroanterior chest roentgenogram shows mediastinal widening of a patient with mediastinal edema, presumably due to watermelon allergy. (*B*) Diffuse esophageal narrowing is seen on the esophagogram. (*C*) Posteroanterior chest roentgenogram 2 days later demonstrates escape of the mediastinal fluid into the pleural spaces.

cases of chylomediastinum in patients who had recently undergone surgical procedures for correction of congenital heart defects. In each case, mediastinal widening occurred before the appearance of pleural effusion, and the mediastinal widening decreased, as the chyle escaped into the pleural space.

When the chylous material leaks into the pleural space, thoracentesis usually establishes the diagnosis. In the newborn, or at other times when the material is not grossly chylous due to lack of ingested fats, indicator dye-tests may be used to document the origin of the fluid.[3]

MEDIASTINAL EDEMA

The rarest cause of acute mediastinal widening is allergic edema. We could find no cases in the literature, but have seen a

57 year old woman who presented with abdominal and substernal chest pain, shock, and mediastinal widening which was presumably secondary to watermelon allergy (Fig. 3*A*). An esophagogram showed diffuse esophageal narrowing without evidence of a tear (Fig. 3*B*). Coincident with the rapid return of the width of the mediastinum to normal was the appearance of large bilateral pleural effusions (Fig. 3*C*), presumably due to leakage of the mediastinal fluid. Examination of the pleural fluid showed an unremarkable transudate with an amylase of less than 50 units. A subsequent skin test with 10,000 units of watermelon antigen caused a large wheal and reproduced the clinical symptoms but not the mediastinal widening. A clinically similar but less severe episode had occurred 3 months earlier, also after eating watermelon.

SUMMARY

Acute, diffuse mediastinal widening is discussed and divided into four groups: hemorrhagic, purulent, chylous and edematous.

Cases demonstrating rare causes, spontaneous hemorrhage and edema due to watermelon allergy are reported. The roentgenographic diagnosis of esophageal perforation is also emphasized.

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METALLIC MERCURY EMBOLI*

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METALLIC mercury is extremely radiopaque and would seem ideally suited to radiologic detection. As far as can be determined, however, the appearance and significance of mercury *in vivo* has not been discussed in the English language radiologic literature.

This report presents 4 cases of metallic mercury emboli which illustrate diagnostic roentgenologic features.

I. PHYSICAL PROPERTIES

Mercury is a silvery metal with an atomic number of 80, an atomic weight of 200.61 and a density (at 37°C.) of 13.50. With a melting point of −38.9°C., it is liquid at room temperature and the only metal liquid at 0°C.[3] Metallic mercury has a high water-metal interfacial tension and will not wet vascular surfaces. When deposited in plasma, therefore, it will round up into a sphere or, if agitated, into innumerable tiny spherules, some of which may later coalesce into larger droplets. Mercury is moderately viscous, but will flow readily through a 22 gauge needle, permitting accidental leakage or self-injection into the vascular system.

Because mercury is denser than plasma, it will flow to dependent portions of the body.

II. PHARMACOLOGY AND TOXICITY

Metallic mercury may enter the body by absorption through the respiratory epithelium and the skin.[3] It may also enter by accidental or deliberate deposition in subcutaneous, intramuscular or intravascular sites. Within the body, the mercury may remain localized for an indeterminate period as a depot of elemental mercury (Hg^0), or it may be oxidized to the soluble mercuric ion (Hg^{++}) and be distributed to other body tissues, principally the kidneys and liver.[1,5,14]

The mercuric ion is toxic. It has a selective affinity for sulfhydryl groups and appears to inhibit enzymes containing such groups.[1] Clinically, this toxicity manifests as mercurialism: metallic taste, excessive salivation, gingivitis, stomatitis, diarrhea and nephrosis.[3] Tremor (Hatter's shakes) and erethism (a personality change characterized by nervousness, timidity, and outbursts of temper) are also significant toxic symptoms.

Excretion is predominantly by the kidney. Elevated levels of mercury in the urine help document *exposure* to mercury, but do not correlate well with *clinical toxicity*.[15]

III. ARTERIAL MERCURY EMBOLI

Arterial emboli result from arterial blood gas sampling with syringes which contain liquid mercury as an anaerobic sealant[7,17] or from arterial pressure monitors which employ a liquid mercury manometer connected directly to an intraarterial needle.[2] Leakage of mercury into the circulation causes peripheral embolization and subsequent transient ischemia or frank gangrene of the distal phalanges.[2,7,17] In addition, the metallic globules incite a local inflammatory reaction which results in the formation of sterile mercury abscesses that may ulcerate and extrude tiny mercury droplets.[7,17] Systemic toxicity is infrequent, presumably because of the small volumes of mercury involved.

Arterial mercury emboli most commonly appear roentgenologically as very finely

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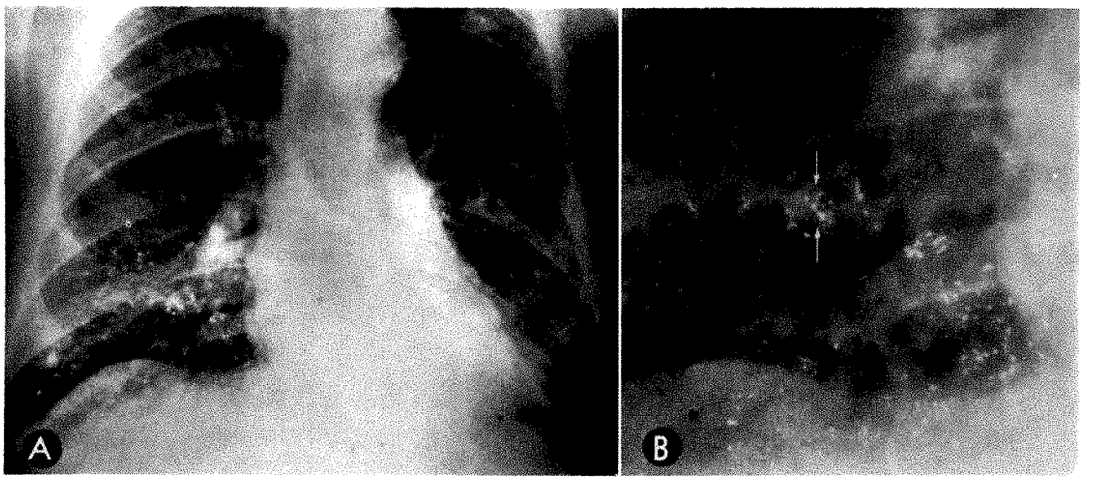


FIG. 1. Case 1. A 67 year old white male immediately post cardiac catheterization. Blood sampling syringes contained liquid mercury as the anaerobic sealant.

(*A*) Chest roentgenogram shows bilateral, discrete, spherical, metallic densities of varying sizes representing mercury pulmonary emboli. (*B*) Detail view of right lower lung shows the branching tubular configuration of a mercury-filled arterial segment (arrows).

divided particles of metallic density in the soft tissues of the distal extremities. These particles may be spherical, fusiform, or splinter-like. Their distribution, as in a patient with involvement of the distal phalanges of the fourth and fifth fingers only (Fig. 6), may suggest a vascular origin. Distinct curvilinear densities conforming to the distal digital vessels and volar arch may be observed occasionally.[2] The major differential diagnosis is extravascular soft tissue mercury deposited by thermom-

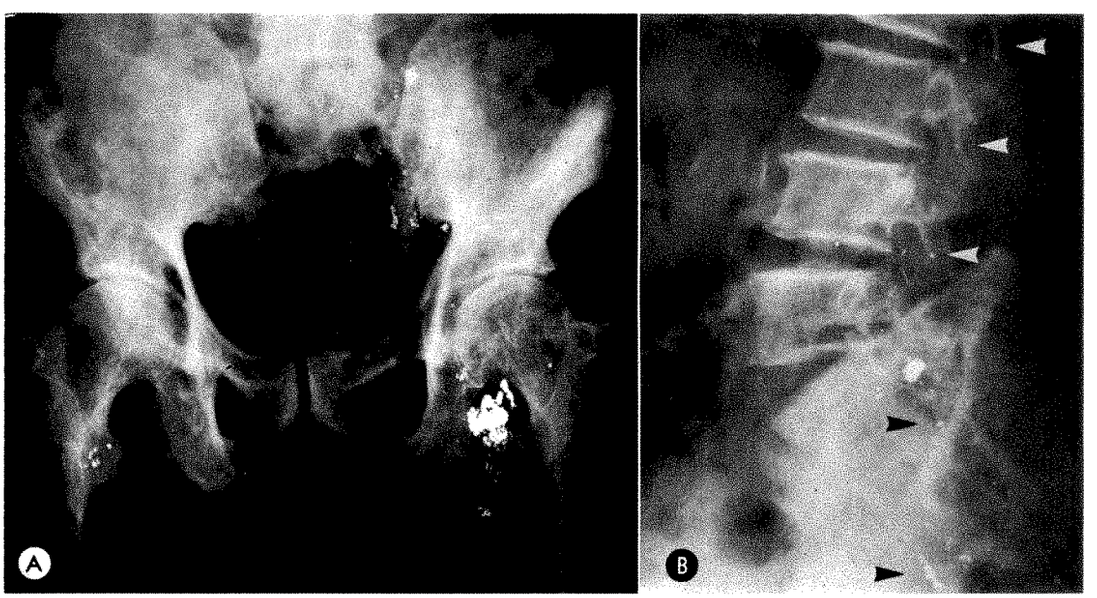


FIG. 2. Case 1. Mercury emboli in the veins draining the left femoral puncture site.

(*A*) Emboli are visualized in somatic and visceral branches of the left hypogastric vein. Groin collections represent perivascular extravasation. (*B*) Lateral view demonstrates emboli in the paravertebral plexus (upper arrowheads) and in hypogastric branches (lower arrowheads).

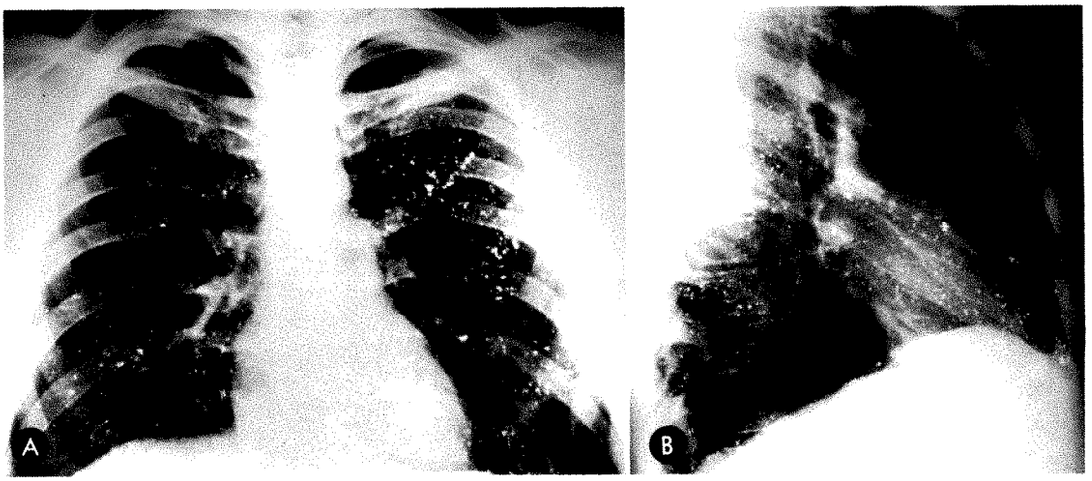


Fig. 3. Case II. A 25 year old black male heroin addict injected metallic mercury into the antecubital fossa "for kicks" 2 years previously. Resection of painful antecubital mass revealed innumerable 0.1 mm. mercury droplets and foreign body inflammatory reaction.

(*A* and *B*) Roentgenograms of the chest show bilateral, scattered and confluent mercury pulmonary emboli.

eter injury[13] or by rubbing the skin with liquid mercury[18] or mercury-containing ointment.[21] Paint-gun injury may be excluded by the particulate nature of the metallic mercury densities and by the clinical history.

IV. VENOUS MERCURY EMBOLI

Venous embolization of mercury results from accidents (laceration of the forearm on a vat of liquid mercury,[9] injury with a broken thermometer[8]), from suicide attempts,[10,16,23] and from venous blood sam-

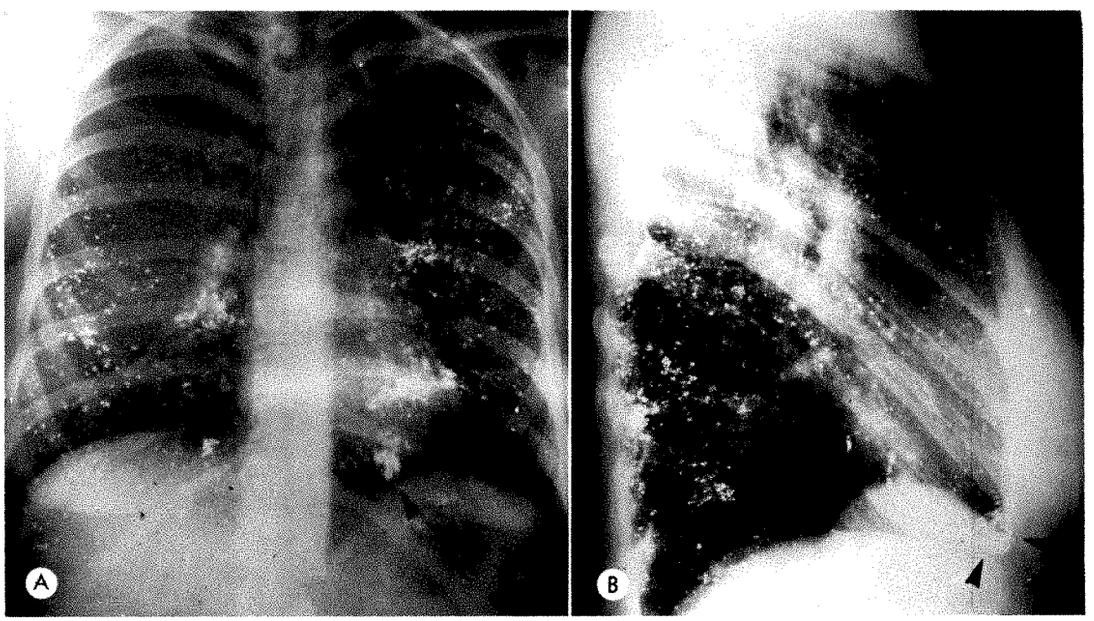


Fig. 4. Case III. A 24 year old black female heroin addict (fiancée of Case II).

(*A* and *B*) Roentgenograms of the chest show diffuse bilateral mercury pulmonary emboli. Mercury has collected at the apex of the right ventricle (arrowheads).

pling utilizing mercury-sealed syringes.[4,19] Buxton *et al.*,[4] for example, cite a 0.9 per cent incidence of mercury pulmonary emboli as a complication of 1,063 cardiac catheterizations and/or blood gas determinations. Symptoms of acute pulmonary embolization and of mercurialism may occur.[4,6,10,16,23]

The roentgenograms of patients with venous mercury emboli are striking. Multiple, tiny spheres of metallic density may be observed throughout the veins draining the entry site: *e.g.*, the pelvic veins and Batson's plexus after femoral vein puncture (Fig. 2, *A* and *B*). Identical spherules may be detected in one or both lungs, either diffusely distributed or restricted to one or several dependent areas (Fig. 1, *A* and *B*; 3, *A* and *B*; and 4, *A* and *B*). These spherules may appear as scattered densities of varying sizes or as beaded chains which conform to the pulmonary arterioles (Fig. 1; 3; and 4). Short tubular structures representing mercury-filled arterial segments will be visualized less frequently (Fig. 1). Mercury may also be noted at the apex of the right ventricle either within the endocardium or as a free intraluminal pool created by coalescence of scattered droplets (Fig. 4).[4,9,11,23]

Because mercury can pass through the pulmonary capillary bed, or around it *via* shunts, mercury may be observed in the pulmonary veins,[10] in systemic sites such as the liver, spleen, thyroid, kidney and brain[4,6,9,12,19] and in the hilar lymph nodes.[10] Since some mercury may extravasate at the entry site, globules of mercury will often be detected in the subcutaneous tissues (Fig. 2, *A* and *B*). Serial roentgenograms of patients with mercury emboli frequently show a decrease in the size and number of mercury deposits with time, presumably because of oxidation of the metal to the soluble mercuric ion.[4,12]

The differential diagnosis of pulmonary mercury emboli is limited by the density, size, and characteristic spherical shape of the mercury droplets. "Bird shot" and shrapnel must be considered briefly, but may usually be ruled out because the particles are larger and more uniform in size than mercury emboli or because they have angular margins. Pulmonary emboli containing opaque media, occurring, for example, after myelography, lymphangiography or hysterosalpingography are less dense than mercury emboli and exhibit a predominantly branching pattern or diffuse haziness. The presence of barium pulmonary emboli after diagnostic enema, of small collections of aspirated barium and of bronchographic contrast material may be diagnosed by their more linear character, by review of previous roentgenograms, and by clinical history.

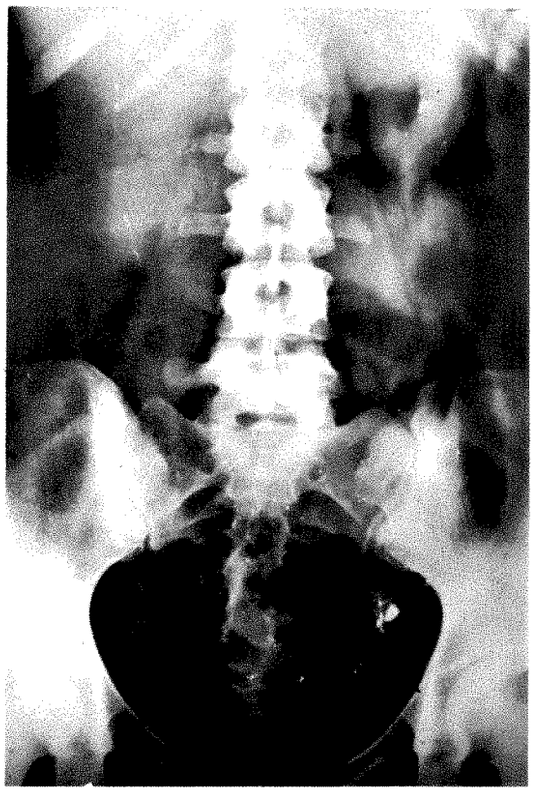


Fig. 5. Case III. Mercury emboli in the pelvic veins and over the renal areas.

Perhaps the most difficult differential diagnosis roentgenologically rests between pulmonary arterial mercury emboli and aspirated intrabronchial mercury, at least 4 cases of which have been reported.[20,22,24,25] Identification of associated intracardiac



FIG. 6. Case IV. A 28 year old white male physician with arterial mercury emboli after brachial artery blood sampling. Mercury from syringe embolized to the dependent fourth and fifth fingers causing transient ischemia and chronic, recurrent mercury abscesses. (Reproduced with permission from *A.M.A. Archives of Internal Medicine*.[17])

mercury, mercury in the abdominal vessels, or mercury in the subcutaneous tissue of the extremities would permit a diagnosis of mercury emboli. The identification of intraintestinal mercury would suggest mercury aspiration. Except for these features, the roentgenologic manifestations of the two conditions may be identical.

V. PATHOLOGY

The pathologic sequelae of pulmonary mercury embolization have been studied in man[8,9,11,12] and experimental animals.[6,10] After embolization, the mercury may remain within the pulmonary arteries, eventually becoming encased by thrombus. Probably as a result of rupture of the capillaries, the mercury may also come to lie within the interstitium and the alveoli.[12] In these locations, mercury abscesses or granulomatous foreign body reactions may develop about each droplet, creating miliary nodules composed of liquid mercury centers and palisaded zones of polymorphonuclear leukocytes, macrophages, and fibrous connective tissue, with or without foreign body giant cells.[6,12] Bronchiectasis with chronic interstitial or alveolar pneumonia may also occur,[6,8,10] as may pulmonary infarction.[10] In general, however, the degree of inflammatory reaction in man has been relatively mild, permitting long survival.

SUMMARY

Embolization of metallic mercury, although rare, does occur.

The pattern of multiple, small, spherical, metallic densities of varying sizes confined to the distribution of one or several vessels is characteristic and permits a reliable roentgenologic diagnosis.

Identification of additional metallic densities in other parts of the body then serves to confirm the diagnosis, define the extent of embolization and indicate the site of entry.

Mercurialism, mercury abscesses, and local ischemia may accompany mercury embolization, determining the patient's presenting complaint.

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ACCIDENTAL INTRAARTERIAL INJECTION IN DRUG ABUSE*

By WILLIAM K. LLOYD, M.D., JOHN M. PORTER, M.D., THOMAS D. LINDELL, M.D., JOSEF RÖSCH, M.D., *and* CHARLES T. DOTTER, M.D.
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RECENTLY, 2 patients were treated at the University of Oregon Medical School for severe tissue necrosis resulting from the accidental intraarterial delivery of self-injected drugs.

What was once an infrequent complication of anesthesia[5,11,13] has become a common penalty of drug abuse.[1,8,12]

REPORT OF CASES

CASE 1. A 37 year old male narcotic addict came to the emergency room approximately 4 hours after having injected an oral preparation of sodium secobarbital (Seconal) into his right radial artery. Immediately following the injection, which consisted of the contents of four 100 mg. capsules dissolved in 2½ ml. of water, the patient had experienced severe pain in the distal forearm and hand. Examination showed cyanosis, coldness, and anesthesia to pinprick of the palm and fingers. The dorsal surface of the hand was spared. There was marked restriction of motion, although pain may have been the limiting factor. The radial and ulnar pulses were strong.

Emergency treatment included morphine sulfate, intravenous dextran 40, and 50 mg. of Lidocaine injected into the radial artery. The pain continued until a right axillary nerve block was instituted. Oral papaverine (100 mg. every 6 hours) and heparin (10,000 units, intramuscular, every 4 hours) were begun, but were discontinued after 7 hours. The axillary block was maintained for the next 5 days. Although at the end of this time the pain had subsided, the hand

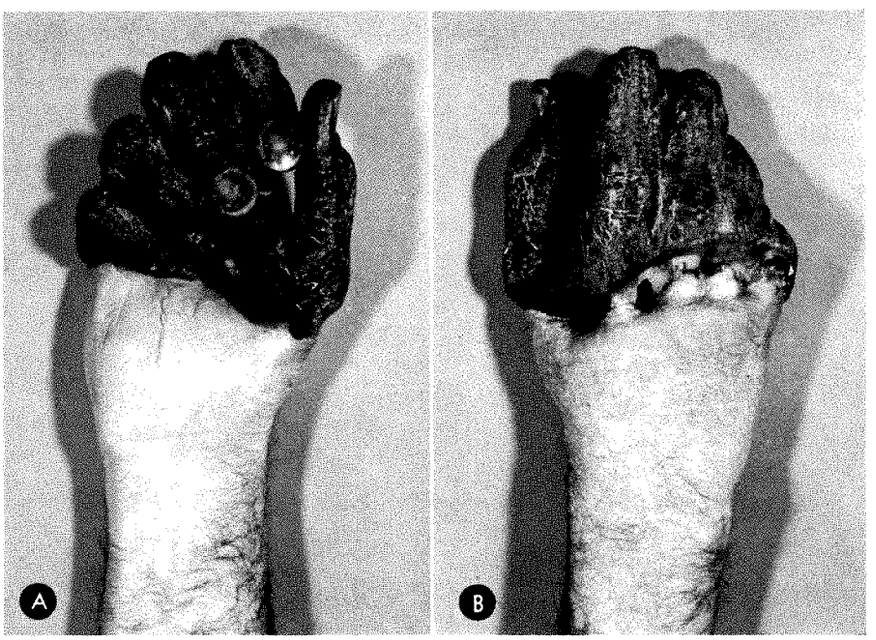


FIG. 1. Case 1. (*A*) Anterior and (*B*) posterior views of the distal right forearm and hand showing mummified digits and open exposure of distal metacarpals.

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Fig. 2. Case 1. Arteriogram of the distal right forearm and hand. (*A*) Arterial phase and (*B*) venous phase. Demonstrated is a complete cut-off of all vasculature distal to the mid-metacarpal level.

and distal forearm had become red, swollen and blistered. Because of this and low-grade fever, antibiotics were started. Thirteen days after the accidental injection, a clear line of black demarcation had formed at the level of the metacarpal-phalangeal joint. Roentgenograms showed no evidence of osteomyelitis. At the end of 1 year, the hand appeared mummified and showed no evidence of either viability or infection (Fig. 1, *A* and *B*). Arteriography revealed complete occlusion of the distal right radial artery and occlusion of all digital arteries at their origins (Fig. 2, *A* and *B*).

Case II. A 32 year old white male accidentally injected into his right radial artery two 50 mg. pentazocine (Talwin) tablets dissolved in tap water. An immediate "burning" sensation in the hand resulted, and over the next 3 days progressive pain, swelling and numbness developed. On the third day, the patient consulted a physician who incised and drained the injection site and evacuated several blood clots from around the radial artery. The patient returned home and was treated with proteolytic enzymes (Papase) and meperidine hydrochloride (Demerol). During the next few days, the hand was intermittently white, pink, and blue-black. Nine days after the accidental injection, the patient was admitted to another hospital because of persistent pain and impending gangrene of the radial side of the wrist and hand.

A stellate block was performed and intravenous dextran 40 and antibiotics were begun. He was referred to the University of Oregon Medical School, where arteriography demonstrated patency of the ulnar and radial arteries and the deep and superficial palmar arcades. There was complete blockage of the digital arteries to the thumb and severely impaired blood flow to the index and middle fingers. Small, irregularly narrowed arteries extended to the fourth and fifth metacarpal phalangeal joints, but no farther. Reserpine, 2.5 mg., was injected through an in-

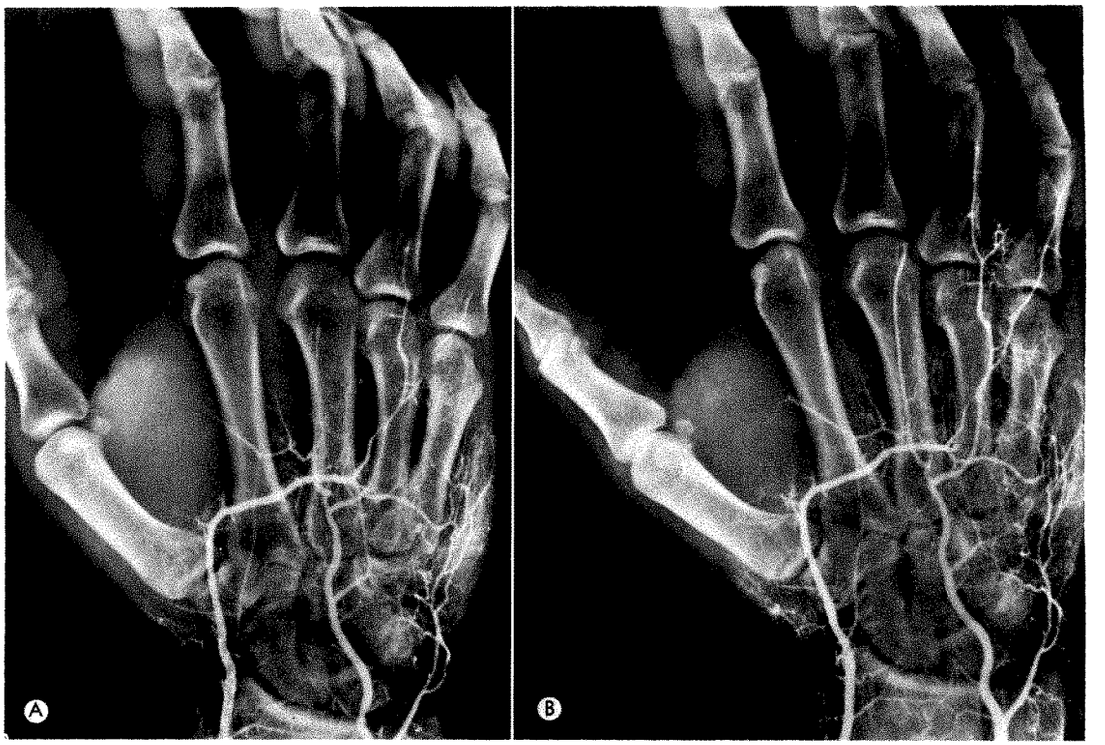


Fig. 3. Case II. (*A*) Arteriogram of the hand prior to reserpine administration. Demonstrated are complete occlusion of digital arteries to the thumb and severely impaired flow to the remaining digits. (*B*) Arteriogram following reserpine administration reveals slightly increased flow to the third, fourth and fifth digits.

dwelling brachial arterial catheter and 24 hours later follow-up arteriography demonstrated increased patency of arteries to the third, fourth and fifth fingers (Fig. 3, *A* and *B*). Despite the intraarterial administration of streptokinase (Streptase, Hoechst), 105,000 units over the course of 19 hours,[6] a third arteriogram revealed no further improvement. The gangrenous thumb and index finger were eventually amputated at the mid-metacarpal level. Microscopic examination of the amputated digits showed extensive gangrene with loss of overlying surface epithelium. Marked endothelial proliferation and luminal narrowing were present in the digital arteries and arterioles. Particulate matter was demonstrated in the lumen of digital small arteries.

DISCUSSION

Van der Post[13] in 1942 described the loss of 3 fingers following accidental intraarterial injection of thiopental. In 1948, Cohen[5] reported 12 similar cases. Prominent clinical features included burning hand pain, shock, vasomotor spasm, cyanosis, mottled bluish-green discoloration, vesiculation, neurologic symptoms and gangrene. It was observed that extremities which became gangrenous were never edematous. It is now clear[8,10,12] that similar complications may follow the improper intraarterial injection of a wide variety of drugs, especially those intended for oral administration.

The mechanisms of injury in such cases have been the subject of controversy. Burn[3] demonstrated a vasoconstrictor action of thiopentone believed due to norepinephrine released from the arterial wall and stated that the effects of thiopentone could be diminished by sympathectomy or prior reserpine administration. Kinmonth and Shepher[9] demonstrated in rabbits that

the vasospasm following intraarterial thiopentone injection was brief and that after a short period of compensatory vasodilatation, normal caliber returned. Later, sometimes as long as 3 or 4 days later, edema, inflammation and vessel occlusion developed; due, they concluded, to direct vascular damage rather than spasm. Since tissue preservation would be favored by maintaining blood flow pending maximal healing, they recommended sympathectomy and heparin. Brown *et al.*[2] showed that barbiturates in the blood in high concentration can form crystals and lead to hemolysis and platelet aggregation. While parenteral solutions of many drugs can be safely given intraarterially, the inert materials and binders contained in tablets of the same drug can cause severe vessel and tissue damage.

Generalized necrotizing angiitis secondary to drug abuse has been described in several recent reports.[4,7] The vascular changes in such cases are widespread and distinctive; representing, we believe, a mechanism of injury different from that which occurred in our 2 patients.

Whatever the mechanism of injury or the roles played by various factors, thrombosis of small or major vessels occurs in all cases where there is permanent tissue damage. Primary treatment should therefore be directed to maintaining blood flow by preventing or limiting thrombosis; thus, even in drug abuse, angiography can play an important role in diagnosis and management.

SUMMARY

Two cases of accidental intraarterial drug injection with resulting tissue loss are reported and the mechanisms of injury discussed.

Although variability in the amount of arterial and tissue damage from case to case and the relatively small number of cases make evaluation of any treatment program difficult, we believe that the use of heparin, intraarterial vasodilating agents and local or systemic fibrinolytic drugs can play important therapeutic roles.

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AUTOTOMOGRAPHY*

By KURT AMPLATZ, M.D.
MINNEAPOLIS, MINNESOTA

A WEALTH of literature has accumulated on laminagraphy which has become a useful and widely employed roentgenographic technique. Autotomography, on the other hand, has received little attention except for scanty reports which contain contradictory and partially erroneous statements. In a recent publication,[4] however, autotomography was again proposed for angiotomography. For several years the use of somersaulting and autotomographic chairs[1,3] has stimulated our interest in this subject.

It is the purpose of this communication to analyze the theory, advantages, drawbacks, and limitations of autotomography. This study was carried out primarily on models and phantoms.

HISTORIC REVIEW AND DEFINITION

Autotomography was first described by Vallebona[5] in 1930. Vallebona was studying the dried skull by moving it in a cradle and obtaining laminagrams, keeping the roentgen-ray tube and the roentgenographic plate stationary. This technique, although extremely simple, was never applied on patients, until Ziedses des Plantes[6] suggested this technique in 1950 for pneumoencephalography. Since then the value of autotomography in conjunction with this neuroradiologic procedure has been well documented in the radiologic literature. The main purpose of this technique is the demonstration of the midline aqueduct by

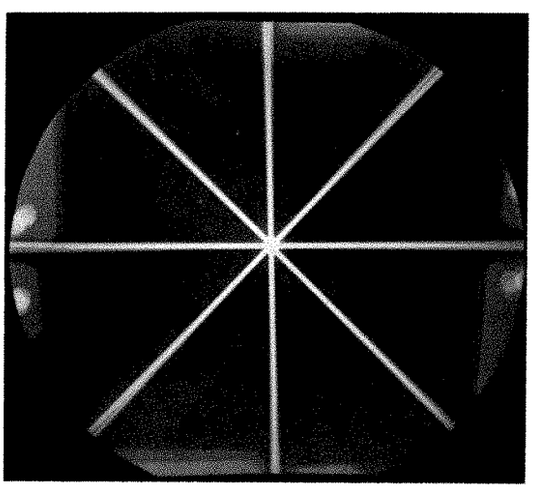


FIG. 1. Autotomogram of a star-shaped wire phantom clearly shows blurring of the wires towards the periphery. Only the very center of the phantom is sharply demonstrated.

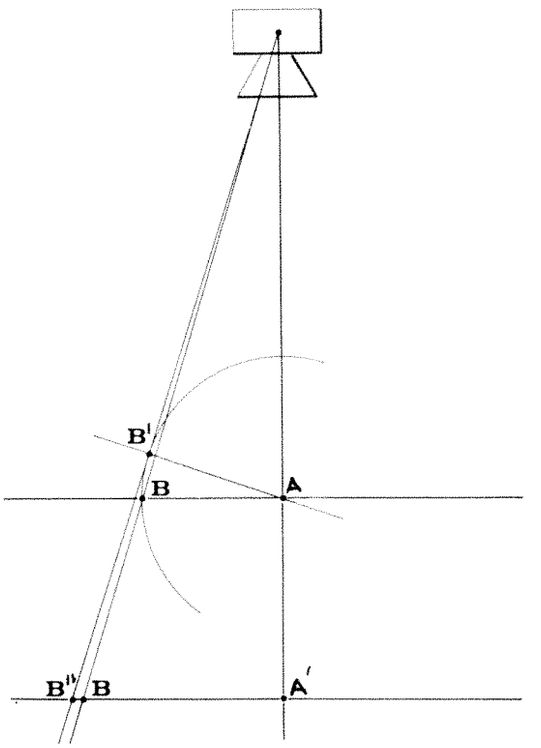


FIG. 2. Basic principle of autotomography. Point B moves to B' during rotation of the body. Its roentgenographic projection on the roentgenographic plate also moves from B to B'', being therefore blurred. A (center of rotation) is projected as A' on the same point on the roentgenographic plate at all times.

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blurring out the dense mastoid areas, by axis rotation of the skull on the odontoid process. The patient was instructed to say "no" by shaking his head or the patient's skull was moved in similar fashion by a sling, pendulum, etc. Since the rotational axis of the odontoid process lies approximately in the same plane with the aqueduct, the aqueduct and fourth ventricle were usually fairly well demonstrated. In 1951 and 1953 Kieffer *et al.*[3] showed that the to-and-fro motion of the skull around the odontoid process could be replaced with a single sweep rotation in a pneumotomographic chair. A smooth, perfect rotary motion was achieved with a pneumotomographic chair. Furthermore, the axis of rotation could be placed anywhere through the cranium, and anteroposterior as well as lateral autotomograms could be obtained. Also, tomography of the skull could be

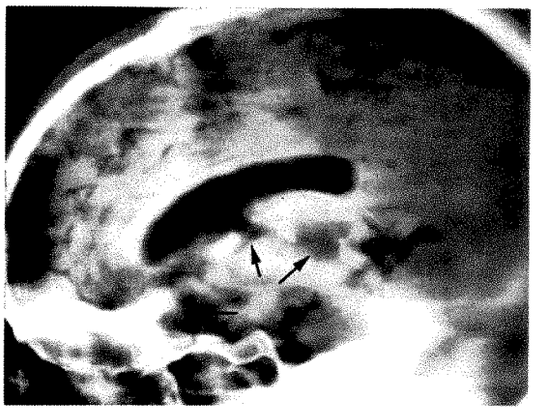


FIG. 3. Small angle autotomogram made with the Amplatz pneumotomographic chair showing excellent sharpness of midline structures and large mass not readily visible in standard views (arrows).

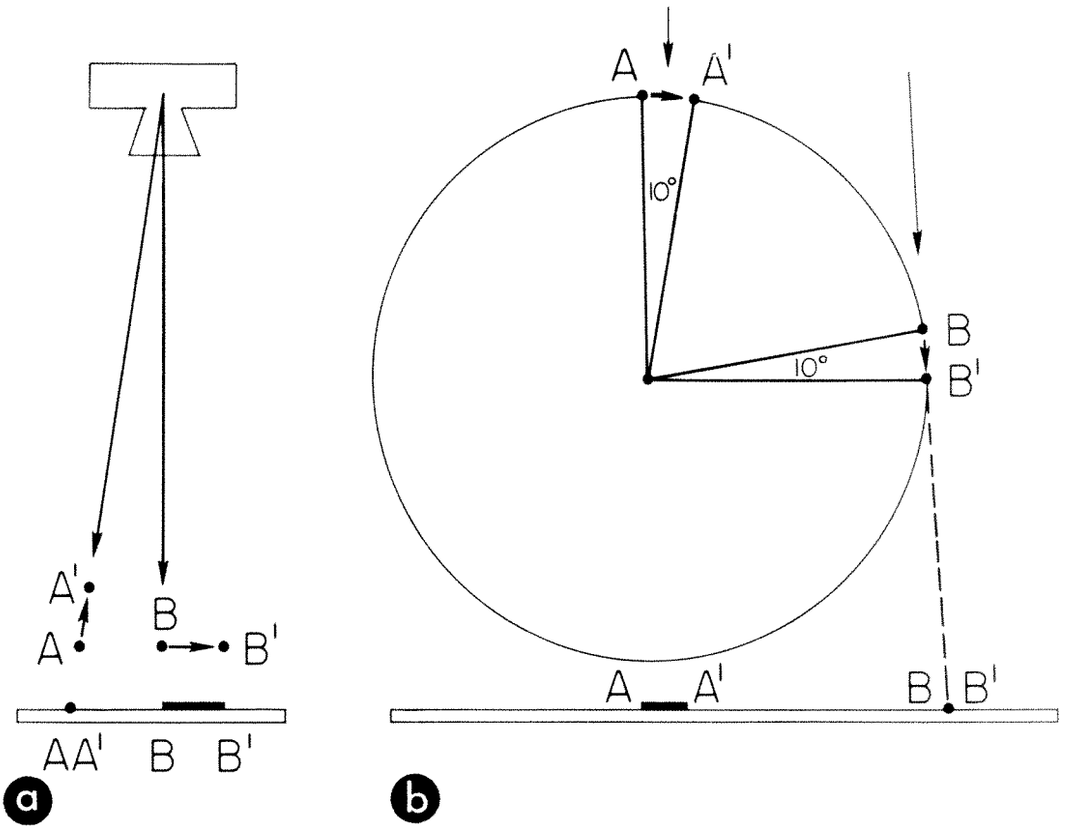


FIG. 4. (*a* and *b*) Diagrams demonstrating points which travel in the direction of the roentgen-ray beam (A to A'). Point A in *a* shows minimal blurring. On the other hand, point A in *b* traveling at a right angle to the roentgen-ray beam shows maximal blurring. Point B traveling in the direction of the roentgen-ray beam to B' shows no significant blurring.

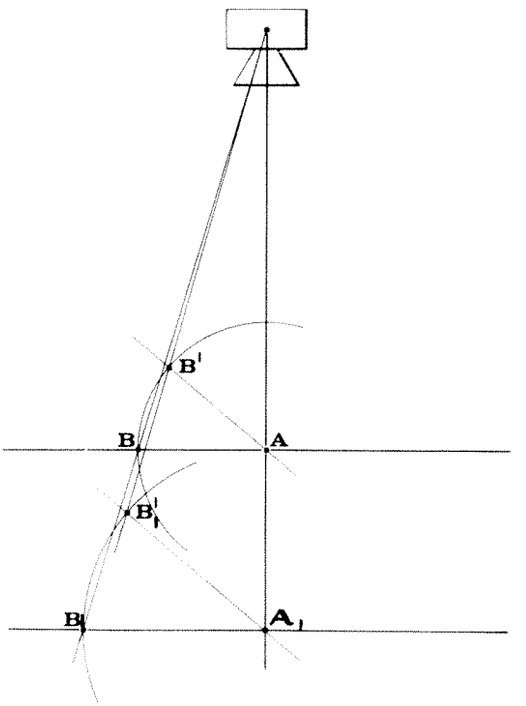


Fig. 5. Diagram of autotomography with motion of the object and the roentgenographic plate. Point B traveling to B′ is projected on the same point on the roentgenographic plate (B1, B1′). Also the center of rotation A is projected on the same point on the roentgenographic plate (A1). With this system a true tomogram can be obtained.

carried out in any position during pneumoencephalography, thus shifting the air to the area of interest. This usually cannot be achieved conveniently with standard tomography which is, therefore, of limited usefulness during pneumoencephalography.

THE ERROR OF AUTOTOMOGRAPHY

A simple wooden model of an autotomograph was constructed, imparting a rotary motion to the object and keeping the roentgen-ray tube and roentgenographic plate stationary. This design is identical to the stratigraph of Vallebona. Autotomography of a star-shaped wire phantom clearly showed that no true laminagraphic layer could be achieved with this apparatus (Fig. 1). Only the very center of the phantom remained stationary, while all wires extending from the center showed motion, thus being unsharply depicted on the laminagram. The degree of motion increased directly with the distance from the center of the phantom. This imperfection of autotomography was proportional to the angle of rotation. For smaller angles of rotation (up to 15°) only a minor unsharpness of structures being distant from the center was noticed.

Basically a tomogram is a summation of a large number of ordinary roentgenograms taken at different angles. However, points lying in the focal plane are projected on the film at the same plane at all times. Therefore, the images of points in the focal plane do not move, being sharply depicted. A simple diagram (Fig. 2) clearly shows that this is not feasible with autotomography since all points in the focal plane are projected on different points on the roentgenographic plate except for the very center. The further away these points are from the axis of rotation, the more motion will occur; consequently, this technique does not fulfill the definition of tomography and could be termed "pseudoautotomography."

Although it is not possible to give a geometrically correct diagram for autotomography which would show points in the focal plane being projected on the same place on a roentgenographic film, excellent laminagrams can be obtained in clinical practice (Fig. 3), particularly if the exposure angles

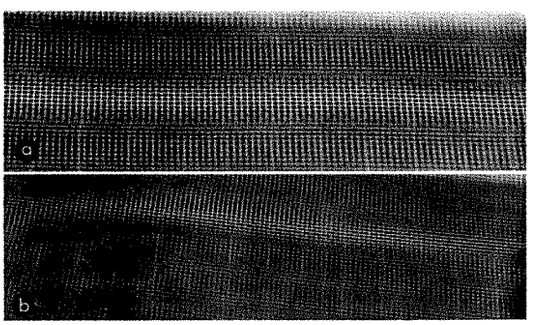


Fig. 6. (*a*) Autotomogram with moving object and plate of wire mesh 45° inclined shows a sharply defined tomographic layer. (*b*) Same wire phantom roentgenographed with the plate stationary shows no tomographic layer except for a zone close to center of rotation.

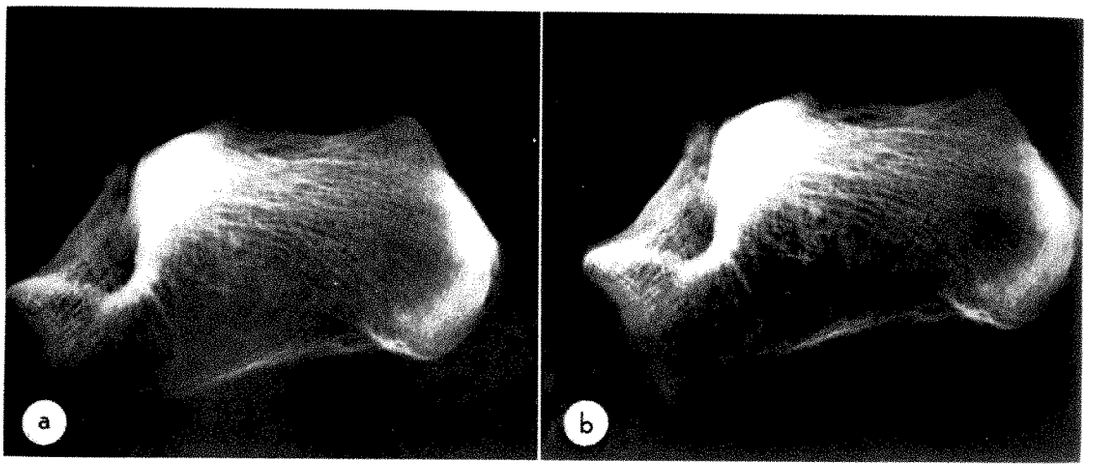


FIG. 7. (*a*) Autotomograms of calcaneus with the roentgenographic plate stationary and (*b*) with the roentgenographic plate moving. Note the significant difference in sharpness of both roentgenographic images, although system A is theoretically wrong. The tomographic angle was 10°.

are kept small as in zonography. Pseudo-autotomography is, therefore, erroneous as far as geometry is concerned but is a practical approximation of true laminagraphy, which is perhaps best understood by a simple diagram (Fig. 4, *a* and *b*). If a point A moves to A′ in the direction of the roentgen-ray beam, it will be projected on the same point on the roentgenographic plate; thus the image will be sharply depicted. On the other hand, if a point B travels at a right angle to the roentgen-ray beam, it will be maximally blurred since the projection also moves from B to B′ on the roentgenographic plate. If a body is rotated in circular fashion 10°, a point A moving at right angle to the roentgen-ray beam will show maximal blurring since its image will travel on the roentgenographic plate from A to A′. Point B, on the other hand, traveling in the direction of the roentgen ray will show minimal if any blurring since the roentgen ray represents the tangent of the circle.

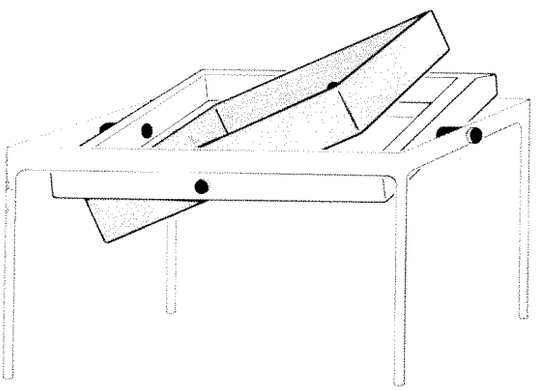


FIG. 8. Two frames rotating perpendicularly to each other allowing motion of the object in 2 planes simultaneously.

In autoplanigraphy, where the object is rotated around a central axis, a pseudo-tomographic layer is accomplished since all points falling on tangents of rotation will travel over a short distance in a straight line in the direction of the roentgen-ray beam. Consequently, the projection of these points on the roentgenographic plate will show no or insignificant motion.

This basic fallacy of autotomography was pointed out by Bozzetti,[2] who suggested to move also the roentgenographic plate in identical fashion to the object. By doing so, all points in the focal plane are projected to the same points on the roentgenographic film at all times, and a true laminagram is obtained (Fig. 5). A model of such an apparatus was constructed, and indeed numerous roentgenograms of a test pattern showed a true horizontal laminagraphic layer. The roentgenogram of a wire mesh placed obliquely at 45° to the axis of rotation was demonstrated as a clear sharp layer (Fig. 6*a*). On the other hand, if the

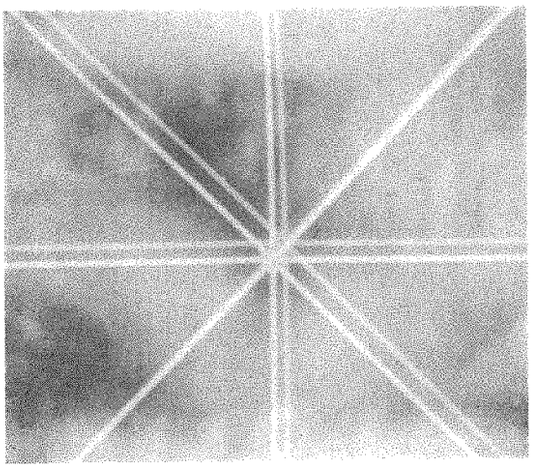


FIG. 9. Star-shaped wire phantom roentgenographed with pluridirectional autotomographic device depicted in Figure 10 shows lack of blurring of 45° diagonal.

roentgenographic plate was kept stationary, according to Vallebona, only the center of rotation showed the true image of the wire mesh (Fig. 6*b*).

However, laminagraphic studies made of various biologic structures, as for example bones, were identical in appearance regardless of whether the technique of Vallebona or Bozzetti was used (Fig. 7, *a* and *b*). These experiments suggest that the degree of unsharpness with autotomography and stationary photographic plate is negligible as long as small angles of rotation are used, and the object is not too large.

By turning the object simultaneously on 2 axes perpendicular to each other, a pluridirectional blurring can be achieved. This was originally suggested by Vallebona in 1930,[5] who proposed to rotate the object in a frame which in turn rotates in another frame (Fig. 8). Such an apparatus was constructed, and identical motion was imparted to the roentgenographic plate, thus achieving true autotomography. Blurring of all structures at right angles occurred, but when a star-shaped wire phantom was placed out of focus and roentgenograms were made, it became obvious that the 45° diagonal was unblurred. Consequently, both simultaneous motions added up to a single linear motion at a 45° angle (Fig. 9). The proposed movement of Vallebona, therefore, did not result in true pluridirectional blurring.

An apparatus of our own design was constructed which imparted a circular motion to the object and to the roentgenographic plate (Fig. 10). True pluridirectional blurring was achieved in all directions. Excellent laminagrams of phantoms and biologic objects were obtained (Fig. 11).

MAGNIFICATION AUTOTOMOGRAPHY

In autotomography the roentgen-ray tube remains stationary. Therefore, no vibration is imparted to the roentgen-ray tube, which is a necessity in all standard laminagraphic systems. Increase of focal spot size due to tube vibration is eliminated, and a 0.3 mm. focal spot tube can be used. Numerous pluridirectional magnification autotomograms were obtained with the designed apparatus yielding excellent results (Fig. 12).

DISCUSSION

Autotomography with stationary roentgenographic plate, although theoretically a

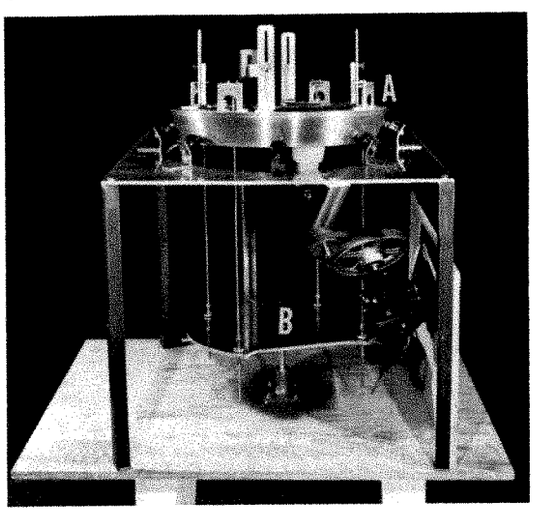


FIG. 10. Pluridirectional autotomograph with the object describing a circular motion on a sphere sector (A) and the roentgenographic plate describing identical motion (B). The large distance between A and B allows 3 dimensional magnification autotomography.

wrong concept, remains a most useful technique for pneumoencephalography using small blurring angles (about 10°). This point was well demonstrated when biologic objects such as bones were examined according to the techniques of Vallebona and Bozzetti (Fig. 6, *a* and *b*). Although the motion suggested by Vallebona is geometrically incorrect, no difference can be detected on the obtained autotomograms provided the angle of rotation is small and, consequently, the layer fairly thick.

One of the major drawbacks of the moving tube system, *i.e.*, roentgenographic tube vibration, is eliminated in autotomography. Consequently, magnification autotomography can be carried out without loss of detail. Mechanically it is simpler to impart a smooth motion to the object and the roentgenographic plate, than to swing the roentgenographic tube, vibration free, through a wide arc. On the other hand, rotation of the body may cause shift of internal organs; consequently, this technique is only suitable for pneumoencephalography, abdominal zonography, intravenous urography, and cholangiography. One of the advantages of autotomography is the possibility of obtaining oblique cuts by angling the roentgenographic plate in relation to the roentgenographic table. By doing so, an oblique zonographic cut can be obtained along the long axis of the kidney, which is usually not feasible with moving tube systems that obtain only tomographic layers parallel to the roentgenographic table top. In standard laminagraphy, both poles of the kidneys are usually not visualized on the same roentgenogram due to the oblique position of the kidneys.



Fig. 11. Three dimensional autotomogram of femur with bone island. Note the extreme sharpness and lack of streaking usually seen in unidirectional tomography.

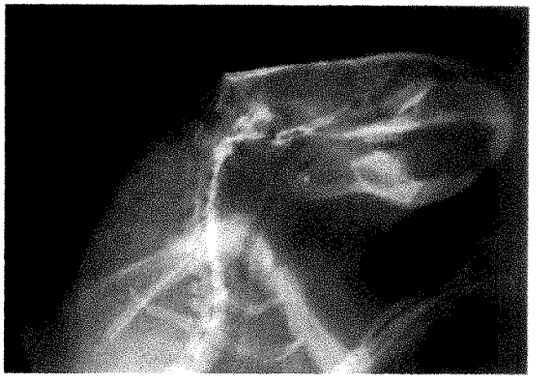


Fig. 12. Magnification (2:1). Pluridirectional autotomogram of the skull of a rat showing excellent anatomic details.

SUMMARY AND CONCLUSIONS

1. The principles of autotomography are reviewed geometrically and experimentally.

2. Autotomography with a stationary roentgenographic plate is geometrically incorrect.

3. With this modality only the axis of rotation shows lack of blurring.

4. With small angles, autotomography yields excellent and sharp images indistinguishable from those of true tomography.

5. Classical autotomography, therefore, remains a very useful technique in pneumoencephalography.

6. True autotomography can be achieved by rotating the object and the roentgenographic plate.

7. This modality has the advantages of preventing vibration of the roentgen-ray

tube. Therefore, magnification tomography can be achieved.

Excellent images were obtained with a new true pluridirectional autotomograph. Its application for clinical use has to be restricted to small angles (up to 15°) because of possible organ shift during rotation of the patient.

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The author is grateful to Dr. Harry Mellins for donating the classic book on tomography by Vallebona.

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A PERCUTANEOUS METHOD OF INTRODUCING THE CAVAL UMBRELLA*

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SURGICAL interruption or compartmentalization of the inferior vena cava has been a life saving procedure in patients with repeated pulmonary emboli. However, the necessity for general anesthesia and operative risk has limited the usefulness of this technique in seriously ill patients.[2,5,8]

Several investigators, therefore, have developed filters which can be introduced into the inferior vena cava from a peripheral vein under local anesthesia. Many devices have been tried experimentally; however, the Mobin-Uddin umbrella has had the widest clinical use and acceptance.[1,3,6,7] So far the device had to be introduced by a jugular vein cutdown, thus again requiring surgery.

It is the purpose of this communication to describe a simple percutaneous introduction technique which can be carried out by radiologists familiar with catheterization procedures. The modified umbrella was successfully introduced percutaneously in various animals.

INSTRUMENTATION AND TECHNIQUE

A human sized M-U umbrella was modified in such a fashion that it could be screwed in an inverted position to the applicator. This was accomplished by cutting a small hole through the center of the umbrella, cutting the end of the loading cone, and shortening the tip of the stylet (Fig. 1, *A* and *B*). With the application of a small amount of medical silicone oil, it is now possible to fit the umbrella into the capsule backwards. This in turn allows introduction of the umbrella and capsule through the femoral vein and forward fixation of the umbrella in the inferior vena cava. The technique is otherwise similar to the jugular approach.

The percutaneous introduction of the large capsule was accomplished through an ultra-thin teflon sheath (I.D. 8 mm., O.D. 9 mm.) which was fitted tightly over a tapered, machined teflon dilator (Fig. 1*C*). Through the central hole of the dilator a standard No. 8 teflon catheter could be passed.

The femoral vein was punctured with a catheter needle in routine fashion, and a No. 8 teflon catheter was introduced. Over the teflon catheter the large teflon dilator, and finally the teflon sheath, were passed allowing introduction of the umbrella containing introducer. Once the desired level in the inferior vena cava was reached under fluoroscopic control, the umbrella was pushed out from the capsule. The umbrella would sping open, and its prongs would engage readily in the caval wall, particularly when aided by a gentle forward push. As soon as the umbrella was well seated, it was unscrewed from the applicator.

In human subjects the following procedure is carried out: (1) introduce a No. 8 catheter into the femoral vein percutaneously; (2) push the teflon dilator and sheath over the catheter into the vein and slightly beyond the iliac bifurcation (application of a silicone lubricant makes the introduction of the sheath easier); (3) pull out the dilator and catheter leaving the outer sheath in place (bleeding can be prevented by elevation of the pelvis); (4) introduce the M-U applicator through the sheath, to about 2 inches below the lower renal vein and extrude the umbrella; (5) keeping the well seated umbrella fixed by gentle forward

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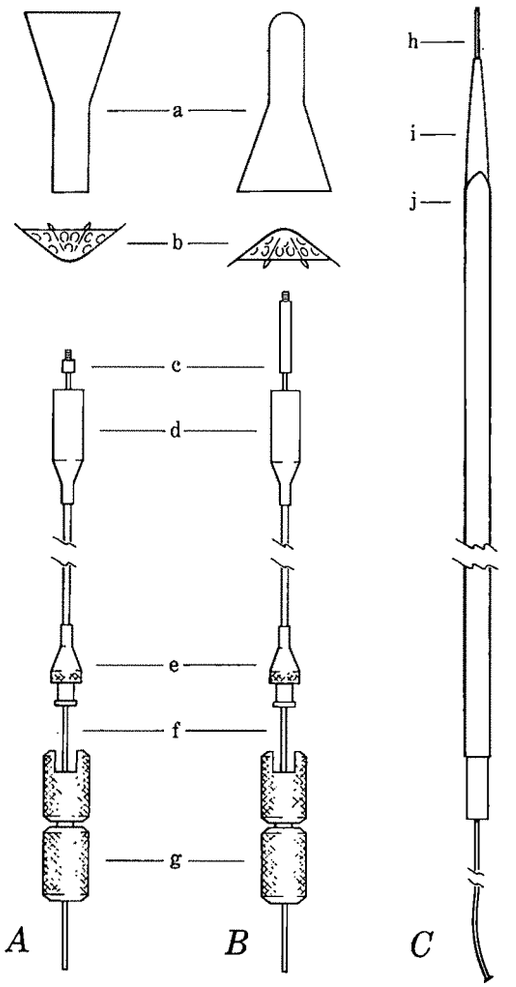


FIG. 1. The Mobin-Uddin umbrella and applicator modified (*A*) for transfemoral insertion and (*B*) as supplied by the manufacturer. (*C*) The venous dilator and sheath. a=metal loading cone; b=umbrella; c=threaded tip of stylet; d=capsule; e=Luer-Lok hub; f=proximal stylet; g=stylet pin vise; h=No. 8 teflon catheter; i=tapered end of venous dilator; and j=external sheath through which the capsule is introduced.

pressure on the introducer, unscrew the stylet and remove the introducer and sheath from the vein; and (6) establish hemostasis by gentle compression at the puncture site and elevation of the pelvis.

MATERIAL AND METHOD

Experiments were designed to answer the following questions: (1) Can the umbrella indeed be introduced in retrograde fashion from the femoral vein and fixed in the inferior vena cava? (2) Is percutaneous introduction of such a large instrument feasible without causing tear and complete disruption of the femoral vein? (3) Would the large hole created in the femoral vein be the site of uncontrolled bleeding requiring surgical closure?

Thirty-one percutaneous introductions of the umbrella were performed in 9 dogs and 9 human cadavers in order to answer the above raised questions.

ANIMAL EXPERIMENT

Large mongrel dogs, 30–50 pounds in weight, were used.

GROUP I; DOGS I–III

The assembly was introduced percutaneously through one or both femoral veins. The umbrella was placed and left in the vena cava. Follow-up venograms were performed at 24 and 72 hours, following which the animals were sacrificed, the veins inspected, and the umbrella recovered and re-used.

GROUP II; DOGS IV–VI

The assembly was introduced percutaneously on one or both sides; 2,000 units heparin were given. The umbrella which had been tied to a wire was introduced, and venograms were taken. About 15 minutes after the introduction, the umbrella was pulled back through the sheath. Follow-up venograms were taken daily until the femoral veins thrombosed.

GROUP III; DOGS VII–IX

The femoral veins in these dogs were surgically exposed, and introduction was performed under direct vision. The animals were then sacrificed, and the veins were inspected.

HUMAN CADAVERS

Because of the absence of blood flow in cadavers, percutaneous femoral vein puncture was only successful in 3 instances. In the remaining 13 introductions, the vein

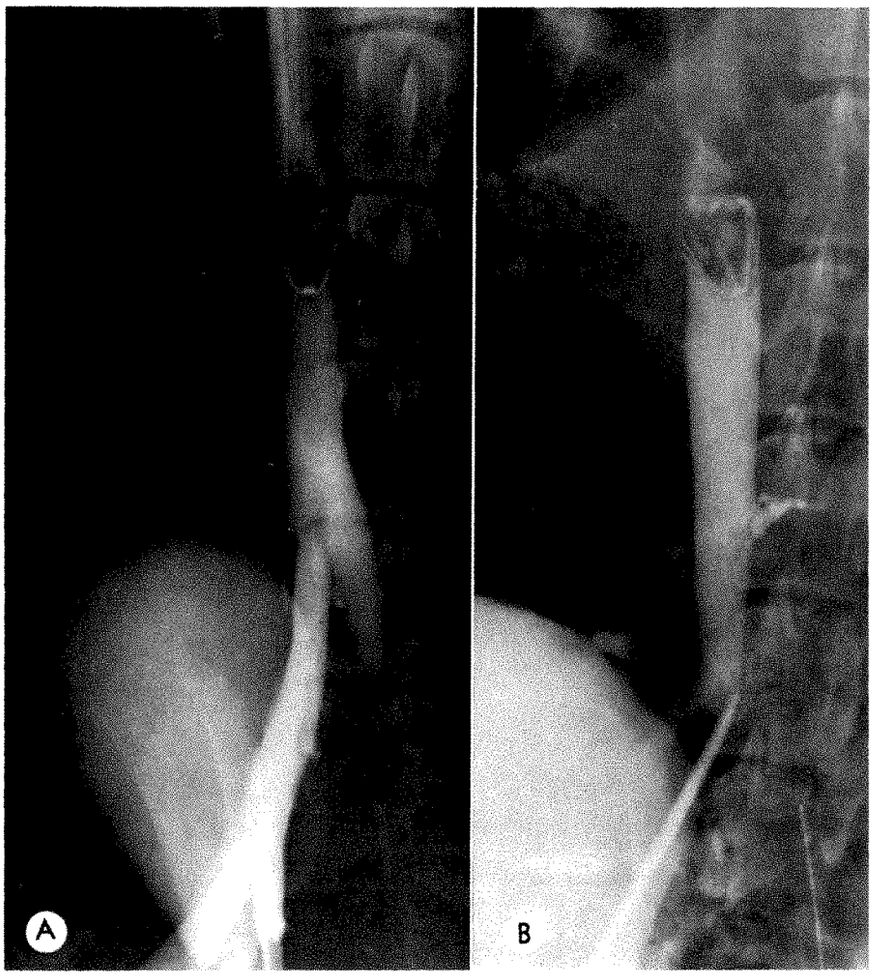


FIG. 2. (*A*) Dog III. Inferior vena cavogram showing a well seated and well fixed umbrella. (*B*) Dog I. Umbrella tilted but well fixed.

TABLE I

RESULTS OF ANIMAL EXPERIMENTS

Dog	Size of Hole (mm.)		Time for Hemostasis (min.)		Palpable Hematoma		Days for Vein to Thrombose (days)		Umbrella	
	Lt.	Rt.	Lt.	Rt.	Lt.	Rt.	Lt.	Rt.	Seating	Fixation
I	5	3	10	5	0	large	1	1	tilted	good
II	—	5	—	7	—	0	—	1	good	good
III	4	3	5	5	0	small	2	2	good	good
IV	—	3	—	5	—	0	—	1	good	good
V	4	3	5	5	0	small	7	1	good	good
VI	3	3	10	15	0	0	1	2	good	good
VII	4	—	—	—	—	—	—	—	—	—
VIII	3	3	—	—	—	—	—	—	—	—
IX	3	3	—	—	—	—	—	—	—	—

TABLE II

RESULTS OF CADAVER EXPERIMENTS

Cadaver		I	II	III	IV	V	VI	VII	VIII	IX
Size of Hole (mm.)	Rt.	5	5	5	3	3	5	4	5	3
	Lt.	5	5	—	3	3	5	—	5	3
Capsule Introduced into Vena Cava	Rt.	no	no	yes	no	yes	yes	yes	yes	yes
	Lt.	no	no	—	no	yes	no	—	yes	no

was punctured after it was isolated as in Group III of the experimental animals.

In the first 7 introductions a short sheath was used, and difficulty was encountered in pushing the capsule beyond the iliac bifurcation. In the remaining 9 a longer sheath and dilator that reached the inferior vena cava were employed.

RESULTS

A. PLACEMENT AND FIXATION

i. Animal. The umbrella was well fixed in the inferior vena cava in all the 6 attempts. In 1 dog (the first attempt), the umbrella was tilted because of the small size of the canine inferior vena cava, but it was firmly fixed (Fig. 2, *A* and *B*).

Three attempts were made to recover the umbrella after fixation, and all 3 attempts were successful (Table 1).

ii. Cadaver. (Table II). When a short sheath was used, the capsule could not be introduced beyond the iliac bifurcation in 6 out of 7 attempts. However, using a sheath that reached beyond the iliac bifurcation, the capsule was easily introduced into the inferior vena cava in 5 out of 5 instances when the right femoral vein was used, and in 2 of 4 instances when the left femoral vein was used.

B. HEMOSTASIS

Animal. Bleeding was easily controlled by gentle compression after 10 introductions. In 1 of the early attempts the wire and catheter perforated the iliac vein 10 cm. beyond the puncture site. Although hemorrhage at the puncture site was controlled, the animal continued to bleed internally and died 24 hours later.

On follow-up (after 72 hours) there were small hematomas (5 cc.) at the site of 2 introductions. The remaining 5 sites showed no palpable hematoma.

C. TRAUMA AT THE PUNCTURE SITE

By direct inspection a hole measuring



FIG. 3. The No. 8 catheter tip points to the hole produced in the isolated femoral vein of a dog after introduction and removal of the venous dilator and sheath.

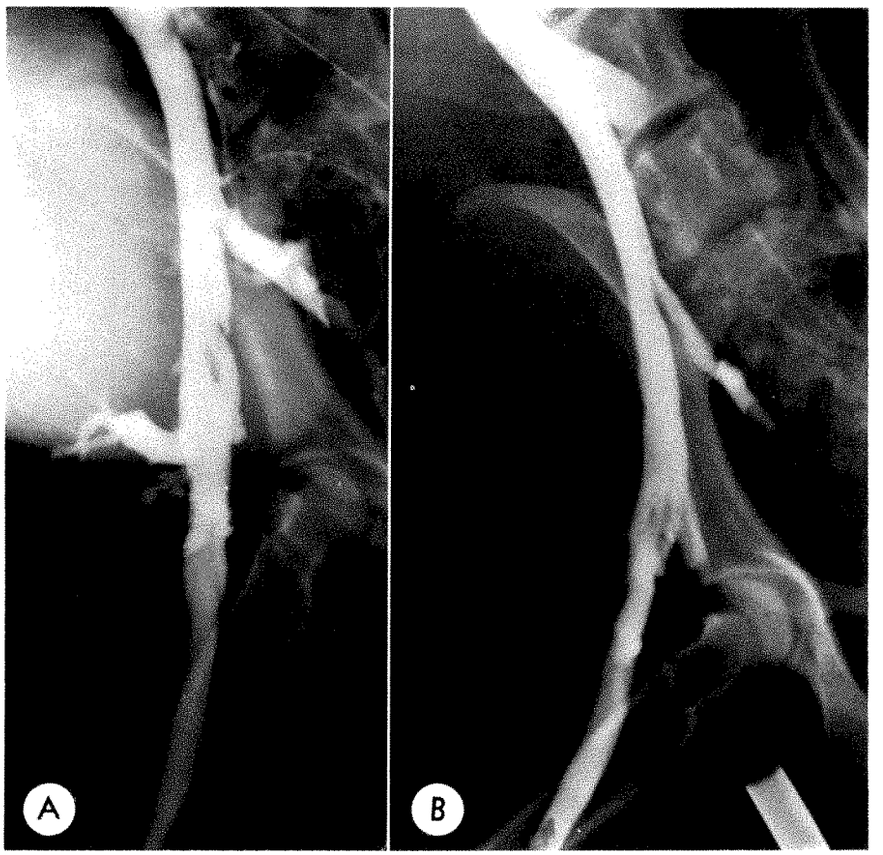


Fig. 4. Venograms on (*A*) Dog I and (*B*) Dog IV 30 minutes after the introduction. Note the size of the capsule in relation to the canine femoral vein.

3–5 mm. was seen at the site of the venous puncture (Fig. 3).

Venograms taken immediately after the introduction showed mild irregularities of the femoral vein at the site of insertion (Fig. 4, *A* and *B*). Follow-up examinations, however, showed that 6 out of 10 veins were thrombosed after 24 hours, 3 out of 10 after 48 hours, and only 1 vein remained patent for 1 week (Fig. 5, *A–C*).

DISCUSSION

Surgical ligation of the inferior vena cava or plication by means of sutures or clips have been an effective mode of preventing clots from reaching the lungs. The surgical risk and complications have been a deterrent to caval plication, and a stimulant to the development of several devices that can be introduced from a peripheral vein under local anesthesia. The Patte intravenous clip and the Mobin-Uddin umbrella appear to be the most promising of these devices. The latter had had a wide clinical acceptance and was thus chosen for this experiment.[3] However, should the Patte clip prove to be as effective and as safe, it would be even more suitable for percutaneous introduction since it requires a much smaller catheter.

The percutaneous introduction is quick and simple, easily carried out by a radiologist and is less traumatic, which is a distinct advantage in a seriously ill patient.

The femoral approach proved to be a feasible route of placing and fixing the

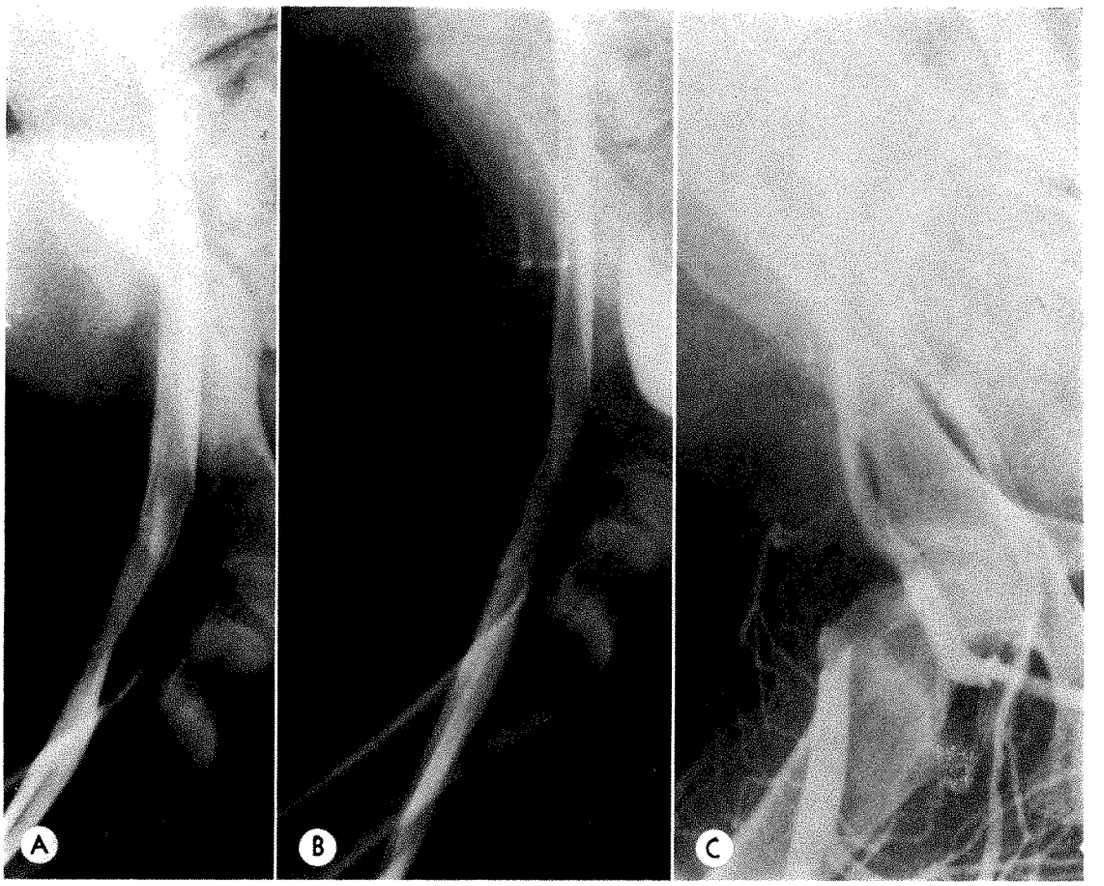


Fig. 5. Dog V. Venograms done (*A*) 30 minutes, (*B*) 24 hours, and (*C*) 1 week after the introduction.

umbrella in experimental animals and human cadavers. This approach allows also recovery of the umbrella if it has been placed too high or too low. Furthermore, the possibility exists to recover the umbrella in an occasional patient who is no longer in danger of throwing pulmonary emboli.

A frequently raised objection to the use of the femoral vein in patients with pulmonary emboli is the fear of dislodging a thrombus. On performing venograms in these patients, we have found the femoral vein to be rarely involved. We frequently use this route to perform pulmonary arteriography and confirm the presence of pulmonary emboli. Prior to the introduction of the catheter, however, a venogram is obtained. The venogram would establish patency of the femoral vein and, in addition, reveal the width of the vena cava and position of the renal veins, which is valuable information for choosing the level of fixation of the umbrella. Furthermore, anomalies of the caval system and unusually large caval veins which may result in umbrella dislodgment will become apparent.

The danger of hemorrhage from the femoral vein puncture site has not been substantiated by our experimental results. As a matter of fact, hemostasis was easily accomplished with practically no hematoma formation which is quite contrary to femoral artery catheterization. The lack of hemorrhage, in spite of the presence of a

5 mm. hole in the venous wall, is very likely due to the low venous pressure. The venous pressure can be reduced to zero by slightly elevating the pelvis or placing the animal in the lateral decubitus position with the puncture site elevated. Under those circumstances, mild external pressure for a few minutes will accomplish hemostasis.

The high incidence of postcatheterization thrombosis in dogs is most likely related to the tendency of these animals to thrombose catheterized veins. The experience in humans, however, would indicate that femoral vein catheterization is well tolerated. Since many of the patients undergoing this procedure would be on anticoagulants, postcatheterization thrombosis should be minimized. If it occurs, it is not a very serious complication, since the umbrella is in place and provides a cover from embolization.

CONCLUSION AND SUMMARY

A simple, percutaneous technique is described allowing the introduction of the Mobin-Uddin cava umbrella via the femoral vein.

Only minor modifications of the original commercially available device are necessary.

On the basis of animal and cadaver studies, the right femoral vein was chosen as a feasible introduction site.

Postcatheterization hemorrhage was not a problem with this technique which is contemplated for human use.

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ADJUSTABLE- *VERSUS* FIXED-FULCRUM TOMOGRAPHIC SYSTEMS*

A MICRODENSITOMETRIC EXAMINATION OF TWO TOMOGRAPHIC SYSTEMS

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THERE are 3 essential elements in any tomographic system; *i.e.*, the x-ray source referred to as the tube or focus; the object; and an image recording system (usually film). A tomographic effect can be created by having any 2 of these 3 elements in synchronous motion at the time of filming. The most common method is to have the tube and film in motion in opposite directions, while the object is stationary. Andrews[1] originally described 6 tomographic methods, 2 of which remain as the basic principles of design of modern tomographic devices. The first technique was originally described as the "planigraphic method" in which the tube and film move with a coordinated movement in planes which are parallel to each other (Fig. 1). The level of the tomographic section is changed by adjusting the level of the point of rotation commonly called the fulcrum. For purposes of convenience, the authors refer to this method as an *adjustable-fulcrum system.* A majority of currently available tomographic devices have been designed upon this basic principle.

The second method was originally described as the "tomographic method" by Grossman.[1] In this instance, the tube and film move with coordinated motion in opposite directions with the tube and film passing through proportional arcs (Fig. 2). The tube-fulcrum and fulcrum-film distances are constant throughout the tomographic movement. The level of section is changed by moving the patient through the plane of focus. This method the authors prefer to call a *fixed-fulcrum system.*

There are no specific units to measure the quality of a radiographic image but quality is primarily controlled by 2 factors: radiographic contrast; and definition or detail. Both of these parameters can be quantitated to predict the quality of the roentgenogram. The present study is an attempt to evaluate the importance of several factors which degrade a simple phantom image within a tomographic system and to compare the degree of degradation in the 2 tomographic systems described: the adjustable-fulcrum system; and the fixed-fulcrum system.

METHOD

Microdensitometric analysis of a line image was selected as the method of choice. It permits a quantitative evaluation of both contrast and detail. In as much as it is not practical to tomograph a slit, the line image was created by radiographing a polished tungsten wire having a diameter of 0.254 mm., a diameter which corresponds to 2 line pairs/mm. The wire was embedded, with an inclination of 1 cm. in 10 cm., in the center of a $5 \times 10 \times 4$ cm. plastic block. Plain film roentgenograms and tomograms of the test object were made throughout both of the tomographic systems and chart tracings of microdensitometric readings were recorded for each image. Analysis of the charted curves permits a quantitation of contrast as well as detail (Fig. 3).

CONTRAST

Contrast can be quantitated as a percentage from the following expression:

* Presented at the Seventy-third Annual Meeting of the American Roentgen Ray Society, Washington, D. C., October 3–6, 1972.
From the Department of Radiology, Guthrie Clinic and Robert Packer Hospital, Sayre, Pennsylvania.

$$\text{Contrast} = \frac{\text{PH} - \text{BH}}{\text{PH}} \times 100,$$

where PH equals the *peak height* and BH represents the *base height.* A totally black image adjacent to a totally white image represents 100 per cent contrast, whereas 2 adjacent images of the same density represent zero contrast. This measurement records the relative differences in density between the center of the image of the wire and background. It is generally agreed that a change of 2 per cent contrast between sharp images may be visually detected. A 5 per cent contrast change can be appreciated within a gradually decreasing contrast field.

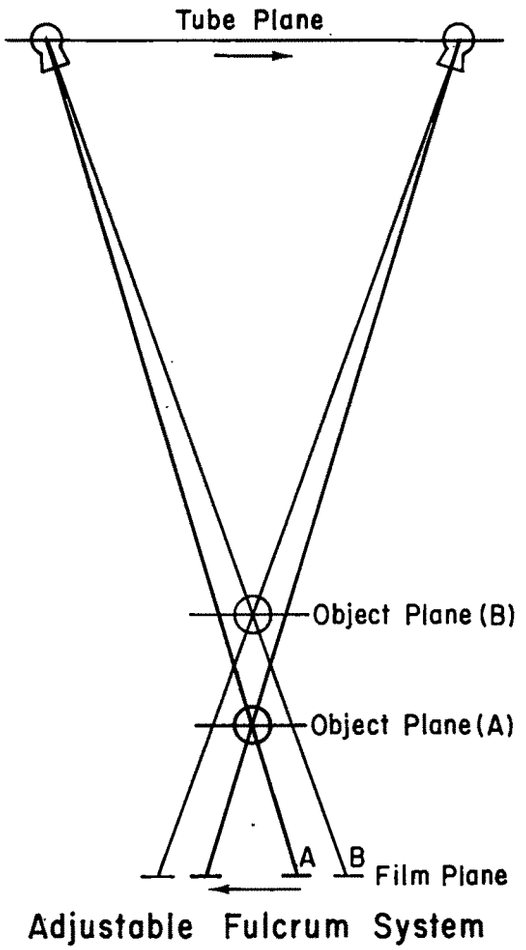


Fig. 1. Line drawing to illustrate a "planigraphic" system.

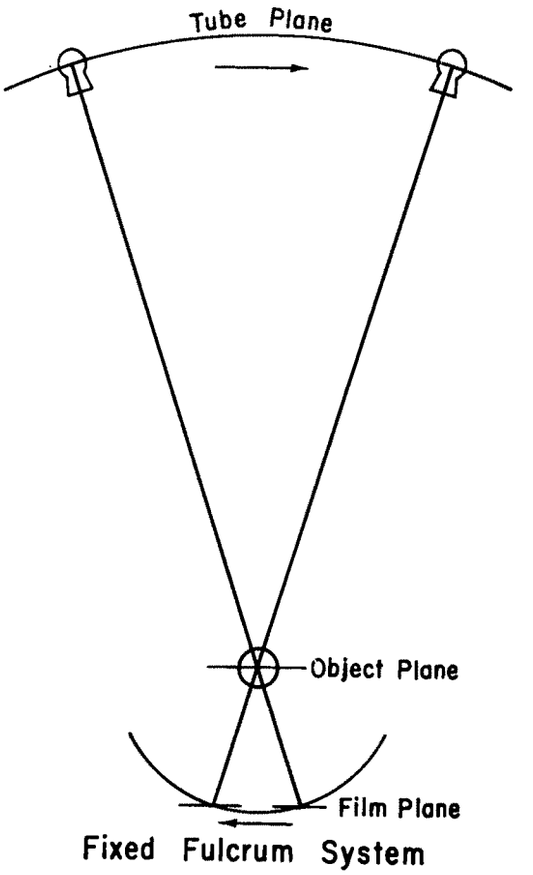


Fig. 2. The "tomographic" system.

DETAIL

Measurement of the full-width of the curve at half-maximum height permits a measure of relative width (actual width plus magnification and distortion) of the image of the wire. The image diameter of the tungsten wire was found to be 0.256 mm. when filming conditions defined zero magnification. This measurement varied by only 0.002 mm. from the actual diameter of the wire, establishing reasonable accuracy of the method.

Examination of the leading slope of the curve (Lateral Deviation at Half Maximum—Fig. 3) provided important information as to the relative unsharpness of the margin of the image.

A record of the measurements from the multiple tracings throughout the study permits a quantitative comparison of the

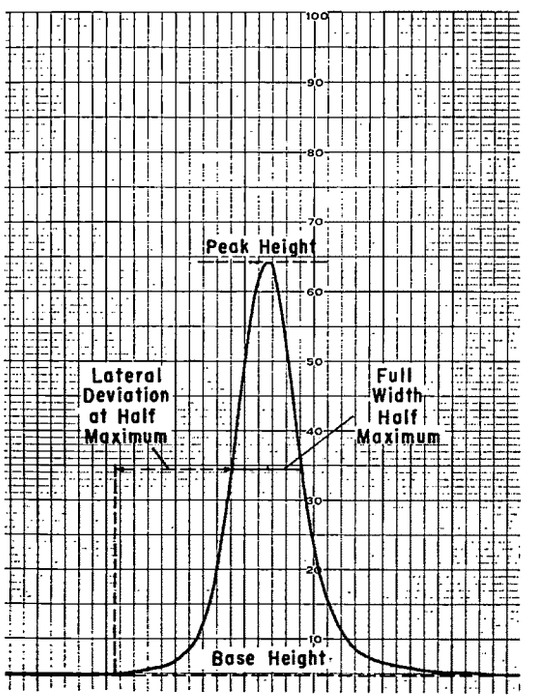


FIG. 3. Typical microdensitometric tracing of a line image.

change in diameter of the image of the wire (line spread function), which, in turn, effects the ultimate resolution, or detail. Figure 4 represents a baseline image from each of the 2 systems together with a 20× magnification of each of these images and their microdensitometric tracings. It is to be noted that the margins of the image are quite sharp, showing only minor differences at 20× magnification between the adjustable-fulcrum and fixed-fulcrum systems.

The deterioration of the image was measured quantitatively and was done so in 10 series of films as follows:

Series I—Baseline image of the object with a 1.0× magnification on single emulsion film.

Series II—Baseline with single emulsion film in the Bucky tray and object at multiple fulcrum positions to define the normal geometry of each system.

Series III—To determine the effect of single emulsion *versus* double emulsion film.

Series IV—The effect of double emulsion film and intensifying screens.

Series V—The effect of focal spot size.

Series VI—A comparison of 8 different screens (examined at low kilovoltage).

Series VII—The effect of high *versus* low milliamperage.

Series VIII—The effect of a cold *versus* hot x-ray tube.

Series IX—Temperature dependence of intensifying screens.

Series X—The effect of some of these variables on the tomograms.

RESULTS

SERIES I. BASELINE IMAGES—TABLETOP

Plain films of the test object were exposed in both systems on single emulsion film at each of the positions shown in Figure 5. To negate the influence of tomographic motion, static films were exposed in all but the tomographic series (Series X). In this series, the test object was placed directly on the film packet on the tabletop thus keeping magnification to a minimum. The fulcrum was adjusted to the midplane of the object.

Contrast. Contrast levels within this series changed only slightly (4 per cent) which is at the margin of the limits of visual detectability (Fig. 6). The change in contrast is probably due to the obliquity with which the primary beam traverses the plastic block and from minimal attenuation of the primary ray by the inverse square law. The change in contrast is negligible at a 20° tube inclination and is greatest with the 40° tube inclination in the adjustable-fulcrum system and at a 48° tube inclination in the fixed-fulcrum system. It is noted that contrast levels are slightly higher in the fixed-fulcrum system and this same contrast persisted throughout the entire study.

Detail. A minor change in image width

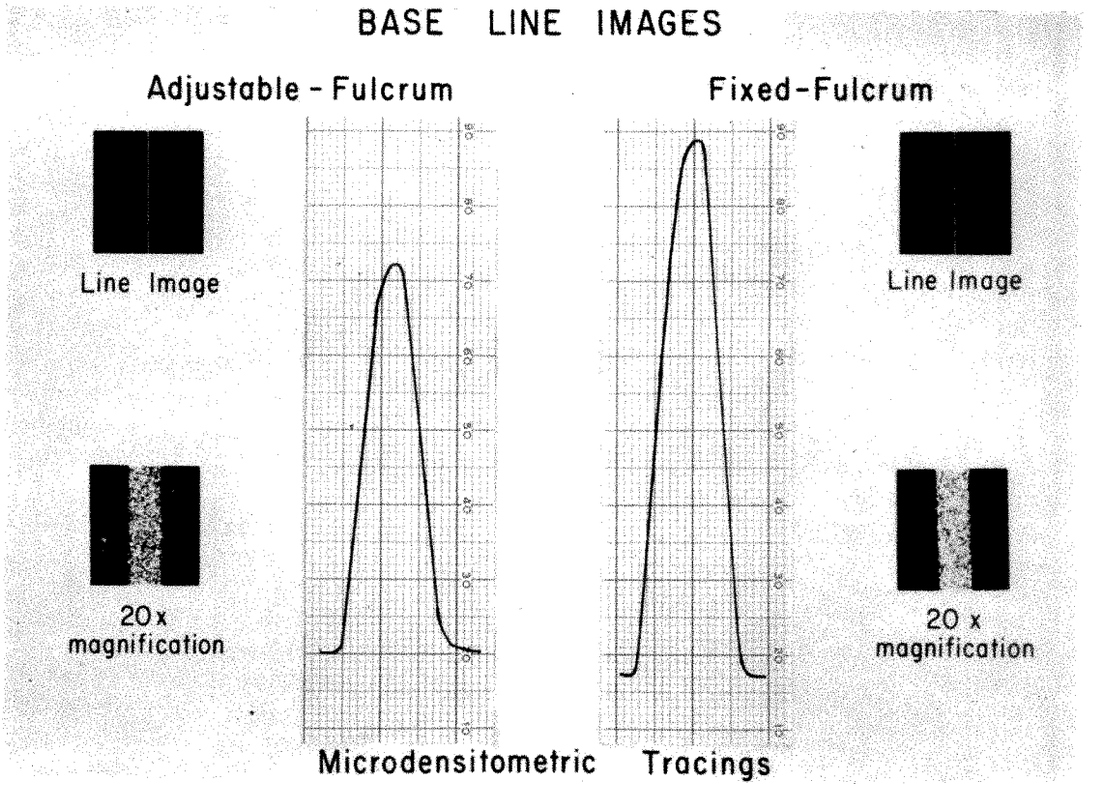


FIG. 4. Baseline images of tungsten wire in both systems with microdensitometric tracings of each.

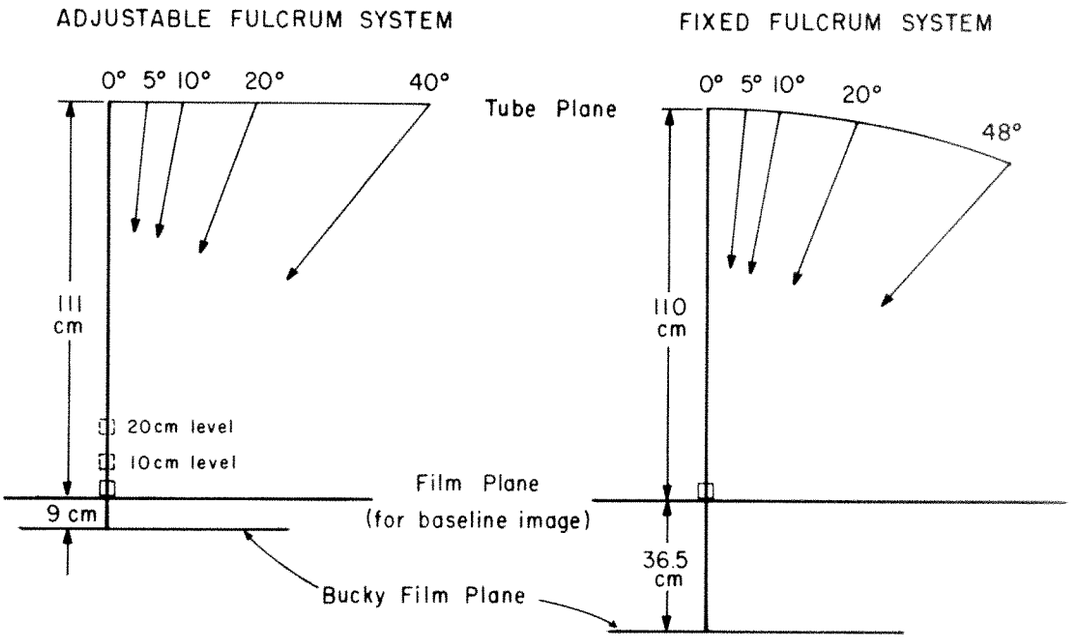


FIG. 5. Line drawing to illustrate the positions from which static and tomographic films were exposed of wire images in both tomographic systems. In the adjustable-fulcrum system, films were exposed from each of the angular settings noted above at each of the fulcrum levels shown.

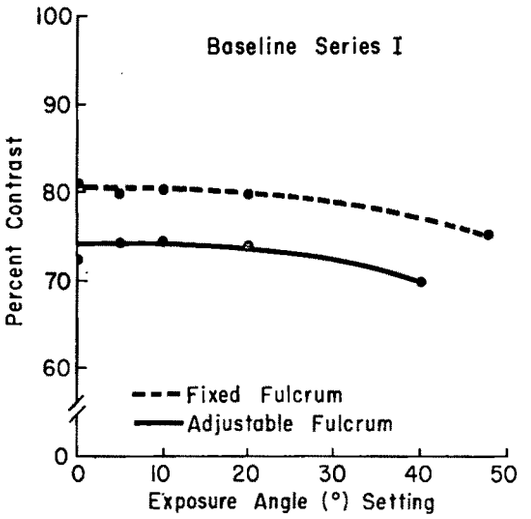


FIG. 6. Baseline contrast values with single emulsion film and 1.0× magnification.

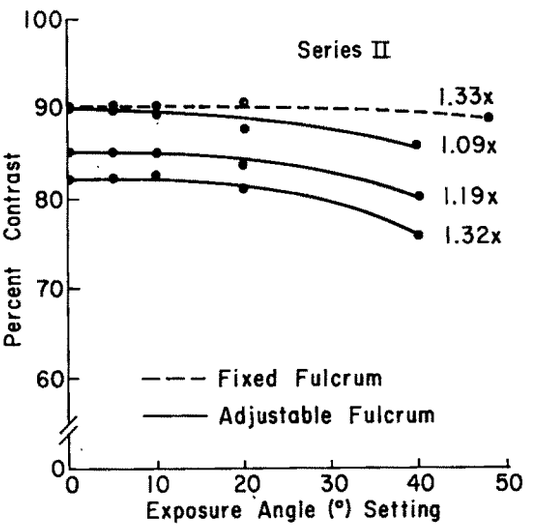


FIG. 8. Contrast change with single emulsion film, and variable geometry in both systems.

is noted in Table 1 and Figure 7. The change in diameter of the wire with change in angle of projection (given here as total sweep angle) is due to distortion and can be calculated from the formula given in Figure 11. Calculation of the total size of the image of the wire at 40° in the adjustable-fulcrum system showed it to be 0.272 mm. This calculated value again is in good agreement with the measured value (0.275 mm.) of the image at 40° confirming the reasonable accuracy of the microdensitometric technique. This initial baseline series without magnification served as the optimal image

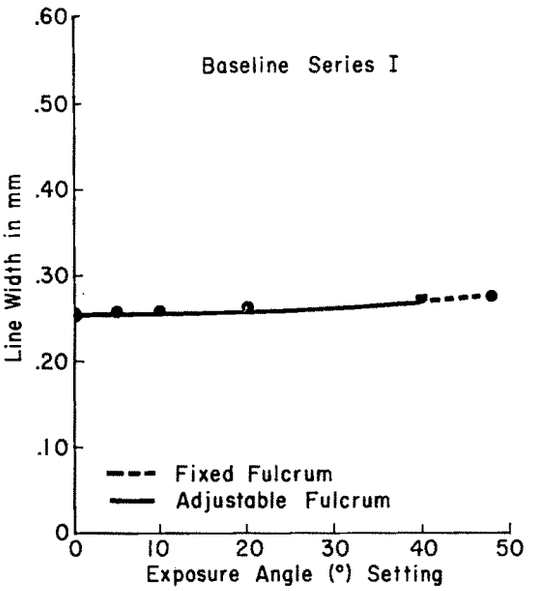


FIG. 7. Line width values with 1.0× magnification showing no difference between the 2 systems. Single emulsion film.

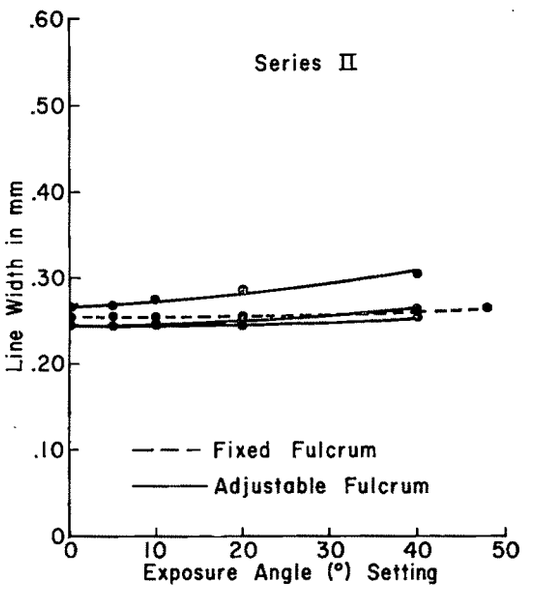


FIG. 9. Line width values for single emulsion film with film in Bucky tray simulating normal system geometry.

Table I

0°	40° (Adjustable-Fulcrum)	48° (Fixed-Fulcrum)
Image diameter in mm.		
0.256*	0.275	0.276

* This microdensitometric reading at 1.0× magnification is in excellent agreement with the actual diameter of the wire 0.254 mm.

to be compared with the images produced in the subsequent series.

SERIES II. BASELINE IMAGES—NORMAL GEOMETRY BOTH SYSTEMS—SINGLE EMULSION FILM

To evaluate the effect of magnification and distortion, plain roentgenograms on single emulsion film were again made throughout the normal geometry of both tomographic systems to evaluate these factors in a static system. This series differed from the initial baseline series only by having the film in the Bucky tray. The object in each instance was located at the fulcrum and plain films were exposed in both systems as follows:

Adjustable-fulcrum	*Magnification*	*Angle*
1. *Phantom and fulcrum at tabletop*		
$\frac{\text{Focus-film distance}}{\text{Focus-object distance}} = \frac{120\text{ cm.}}{111\text{ cm.}}$	= 1.09×	0°, 5°, 10°, 20°, 40°
2. *Phantom and fulcrum 10 cm. above tabletop*		
$\frac{\text{FFD}}{\text{FOD}} = \frac{120\text{ cm.}}{101\text{ cm.}}$	= 1.19×	0°, 5°, 10°, 20°, 40°
3. *Phantom and fulcrum 20 cm. above tabletop*		
$\frac{\text{FFD}}{\text{FOD}} = \frac{120\text{ cm.}}{91\text{ cm.}}$	= 1.32×	0°, 5°, 10°, 20°, 40°
Fixed-fulcrum		
1. *Phantom at the fulcrum*		
$\frac{\text{FFD}}{\text{FOD}} = \frac{147.6\text{ cm.}}{111.1\text{ cm.}}$	= 1.33×	0°, 5°, 10°, 20°, 48°

This series of films provided an evaluation of image quality within the changing geometry of the 2 systems and represents the most important phase of this study.

Contrast. In the adjustable-fulcrum system, only minor change in contrast is noted at levels below 20° and for wide angles below a 10 cm. level, whereas 14 per cent reduction is noted at 40° when the level of section is raised to 20 cm. (Fig. 8). In the central axis, a maximum change in base contrast from 90 per cent to 76 per cent is noted as the table is raised to the 20 cm. level. This magnitude of contrast change may be important when long series of films are exposed through the diameter of the chest, for example, and particularly so when thin sections are made employing wide angles. The curves charted in Figure 8 represent the contrast changes for images projected to the center of the film. Further deterioration of contrast can be expected to appear as the object is displaced to the margin of the film and this aspect will be considered in greater detail later in the text.

In the fixed-fulcrum system, only a 2 per cent change in contrast is noted (Fig. 8). This minor change will be constant throughout the system and will not be detectable in the resulting tomograms.

Detail. The adjustable-fulcrum system showed only a minor change of 5 per cent in image size (0.012 mm. at 40°) when the phantom and fulcrum are at the tabletop (Table II; Fig. 9). Again, this is a factor of distortion to be described in greater detail later.

At 10 cm. above the tabletop, a 10 per cent increase in size is noted at 40°, while a 14 per cent increase is noted at the 20 cm. level. The percentage increase in size is not proportional to the magnification one would anticipate from a simple calculation of M = FFD/FOD. The latter assumes a point source of the x-ray beam which also will be considered in greater detail later in the text.

Only a minor change in object size (2.3 per cent) is noted in this series in the fixed-fulcrum system (Table II; Fig. 9).

TABLE II

	0°	5°	10°	20°	40°	48°	
Adjustable-fulcrum	Line spread in mm.						Per cent
Phantom— 0 cm. 1.09×	.244	.244	.244	.244	.256		5
Phantom—10 cm. 1.19×	.244	.244	.247	.250	.268		10
Phantom—20 cm. 1.32×	.268	.268	.275	.288	.305		14
Fixed-fulcrum							
Phantom at fulcrum 1.33×	.256	.256	.256	.256		.262	2.3

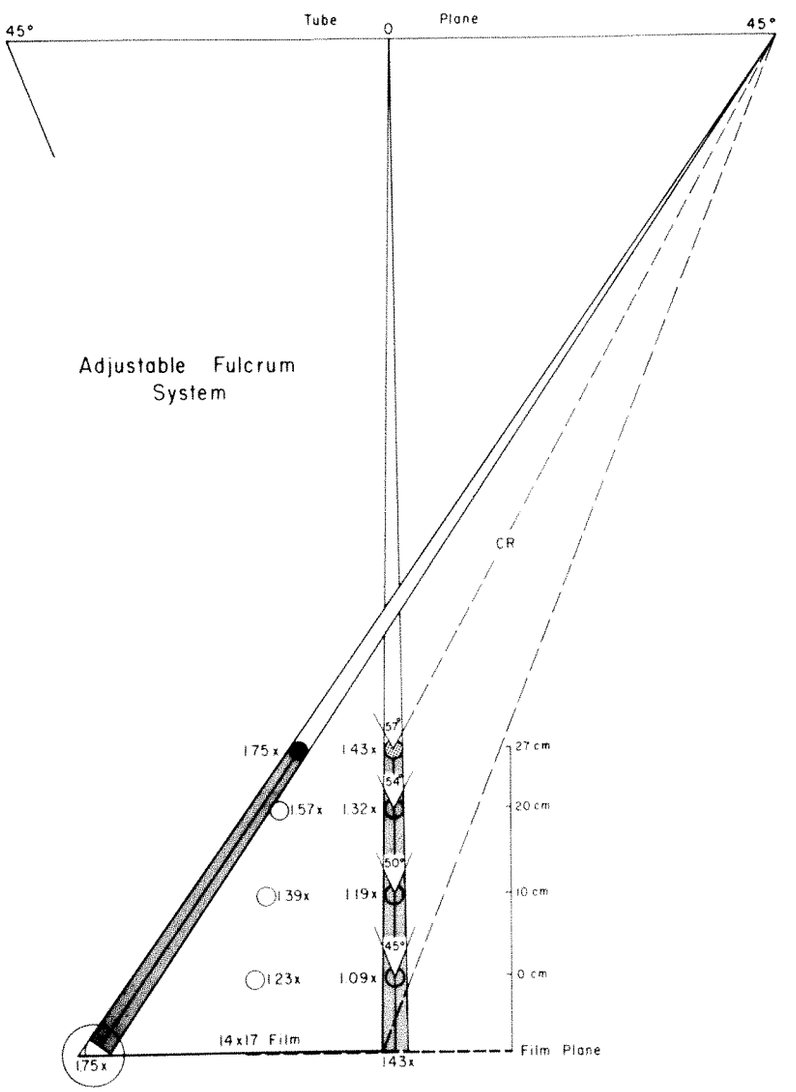


FIG. 10. Drawing to illustrate the geometry at 4 fulcrum levels in an adjustable-fulcrum system. Central axis and off-axis magnification is also shown.

All of the above considerations of detail degeneration will be accentuated as the object moves from the central axis of the field to a more lateral position. This phenomenon can only be appreciated by a precise examination of the geometry of the 2 tomographic systems.

The changing geometry of the adjustable-fulcrum system proves to be extremely important. Figure 10 is a schematic representation of an adjustable-fulcrum system showing the possible positions of the object and fulcrum from 0 cm. to 27 cm. above the tabletop. These values are also given in Table III. The magnification factors at the mid-axis of the system are noted as well as the extremes of distortion from an off-axis object which would be projected to the lateral margin of a 14×17 inch film. In the central axis at the tabletop, there is a magnification of 1.09×, whereas at the extreme off-axis position, even at the tabletop, there is a magnification of 1.23× from distortion. At the 10 cm. level, magnification in the central axis becomes 1.19× and off-axis, 1.39×. At the 20 cm. level, central axis magnification is 1.32× and at the extreme off-axis position at this level, it is 1.57×. At the upper extreme of this tomographic system at the 27 cm. level, the magnification in the central axis is 1.43× and at the extreme off-axis position, it is 1.75×.

Total magnification equals magnification plus distortion and can be calculated from the formula given in Figure 11.

The reason for the significant increase in distortion in the adjustable-fulcrum system is occasioned by the fact that the angle of section (a′) increases as the fulcrum is raised above the tabletop. When a 45° angle is selected from the control panel, a 45° angle exists only at the tabletop. This angle increases to 57° when the fulcrum is raised to the upper limits of the tomographic system (Fig. 10). The angular change is due to the fact that, as the fulcrum is raised, the tube remains at a stationary position, but the Bucky tray moves laterally to accommodate the change in position of the fulcrum. The focal film distance increases and the tomographic angle changes with each change in level. *It is extremely important that the radiologist be cognizant of this increase in magnification as the fulcrum is raised above the tabletop in an adjustable-fulcrum system and, also, of the increasing distortion as elements of the object are displaced from the central axis of the system.* One augments the other to produce significant magnification distortion at the higher and more lateral positions of an adjustable-fulcrum system.

The relative effect of off-axis distortion is significantly less in a fixed-fulcrum system (Fig. 12). Here only one fulcrum position is considered at which point there is

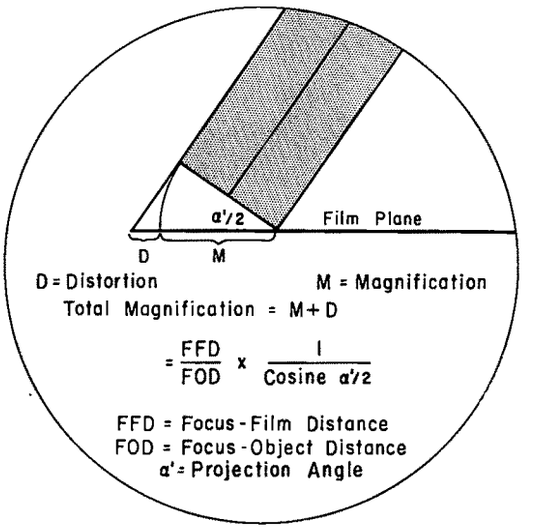


Fig. 11. Diagram to illustrate image deterioration and formula for calculation of total magnification by geometric distortion.

Table III

	Central Axis	15 cm. Off-Axis
Adjustable-fulcrum	Magnification	Magnification +distortion
Level of section		
0 cm.	1.09×	1.23×
10 cm.	1.19×	1.39×
20 cm.	1.32×	1.57×
27 cm.	1.43×	1.75×
Fixed-fulcrum	1.33×	1.50×

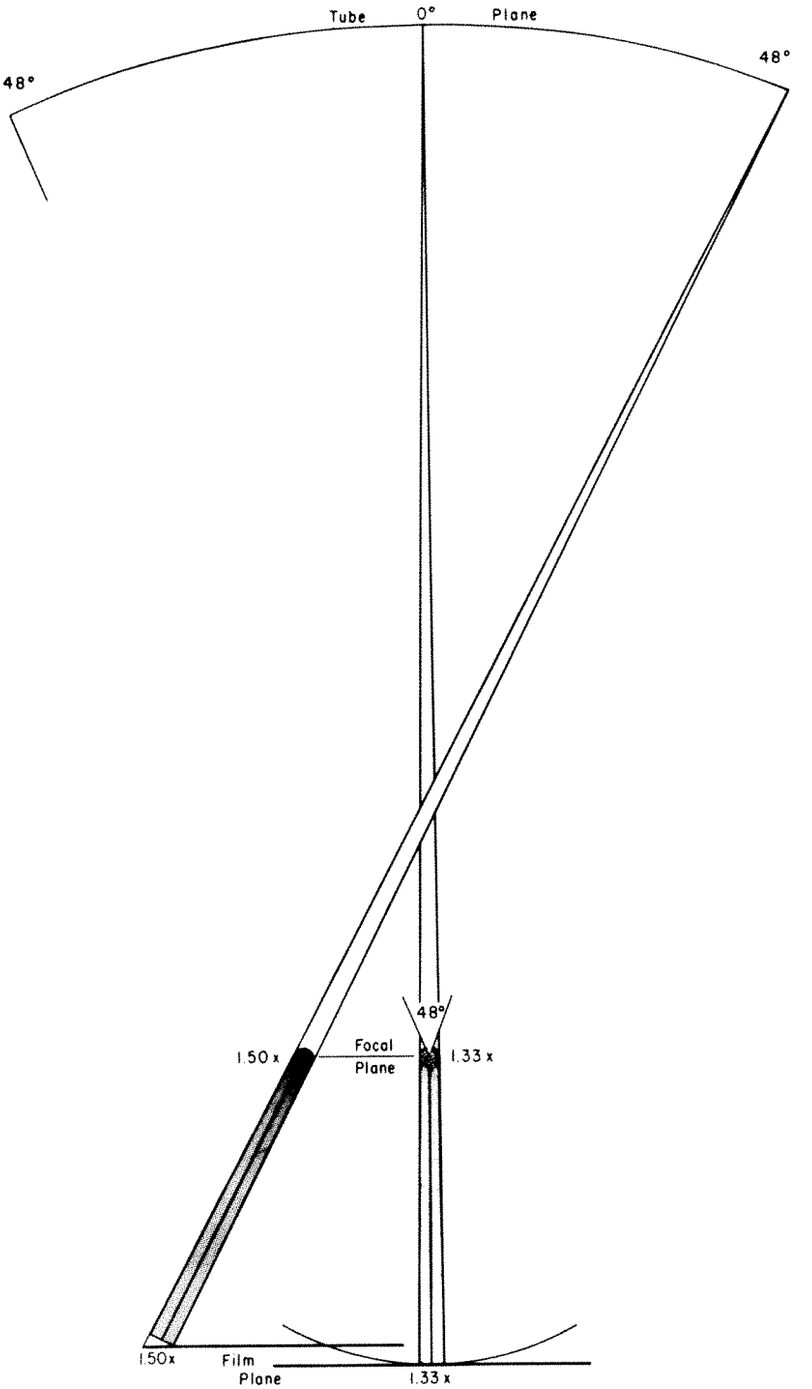


FIG. 12. Diagram to illustrate the geometry of a fixed-fulcrum system.

1.33× magnification in the central axis of the film and this becomes 1.50× magnification at the most lateral position of a 14×17 inch film at the maximal angle of 48°.

In compound tomographic movements,

any off-axis object element will experience variable magnification and distortion during the tomographic movement, producing an inherent unsharpness of the tomographic image. In light of the above considerations, this phenomenon is potentially much more significant in the adjustable-fulcrum system than it is in the fixed-fulcrum system. In general, inherent unsharpness of the tomographic image is most significant at lateral positions higher in the tomographic system.

SERIES III. SINGLE EMULSION *VERSUS* DOUBLE EMULSION FILM

The image characteristics of double emulsion film (Cronex 4) were compared with the single emulsion film used in the baseline series (Kodak single-coated blue sensitive #SB54) by repeating Series II with Cronex 4 double emulsion film. A difference in image quality might be expected on 2 theoretical grounds: a difference in the depth of the image recording system; and the density.

The relative dimensions of single emulsion *versus* double emulsion film can be appreciated from Figure 13. The thicknesses of the image recording systems are .0005 inches for single emulsion film and .008 inches for double emulsion film. Image distortion will change as the angle of the incident ray changes being greater when wide angle exposures are employed. Considering these 2 variables (angle of section and depth of imaging system), Fagerberg[3] has offered a simple equation to predict unsharpness as follows:

$$X = K\ (\tan a'),$$

where X=image unsharpness (X_1 or X_2, Fig. 13), K=depth of recording medium, and $a' = \frac{1}{2}$ amplitude.

When the tube is perpendicular to the film, there will be no image system unsharpness. When the tomographic angle is 40°, the anticipated unsharpness is negligible with single emulsion film: X=.0005 (tan 40°/2); X=.0005×.364; X=.0002 inches; and X=.005 mm.

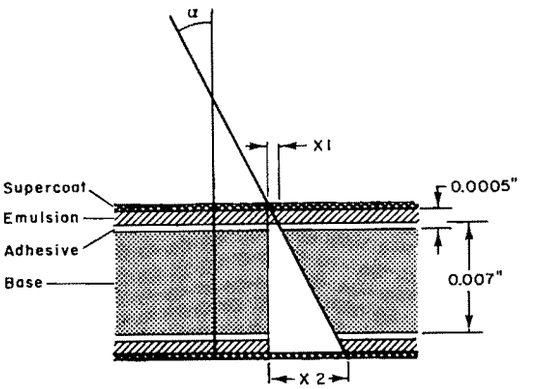


FIG. 13. Cross section of single emulsion *versus* double emulsion film showing possible image distortion from film thickness. ×1 represents single emulsion distortion and ×2 double emulsion film distortion.

Maximum unsharpness in either tomographic system with double emulsion film may be anticipated at:
X=.008 inches (thickness of double emulsion film)×tan 57°/2 (the maximal angle of 57° occurs in the adjustable-fulcrum system at a 27 cm. level); X=.0043 inches; and X=.109 mm.

A change in density may be expected since the total density exhibited by the roentgenogram is the sum of the density of each emulsion.

Contrast. Review of the microdensitometric tracings showed no significant change in contrast. The levels (Fig. 14) were identical with those in the single emulsion film throughout the series in the adjustable-fulcrum system. The levels are slightly higher in the fixed-fulcrum system, but not enough to be significant with contrast difference of less than 2 per cent.

Detail. Minor change in image size is noted (Table IV), but the change is not sufficient to affect the resolving power of the system. The change is greater at a 20 cm. level in the adjustable-fulcrum system as might be expected from the previous discussions of the change in geometry.

It can be reasonably concluded that there is no significant change in contrast or detail in either tomographic system by the use of double emulsion film. The theoretical

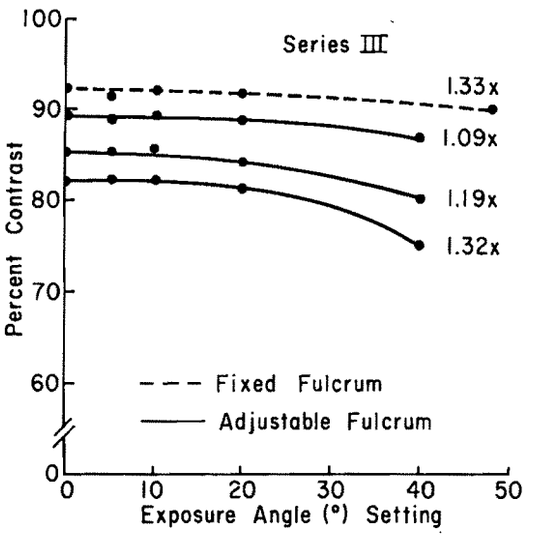


FIG. 14. Contrast levels of both systems with double emulsion film.

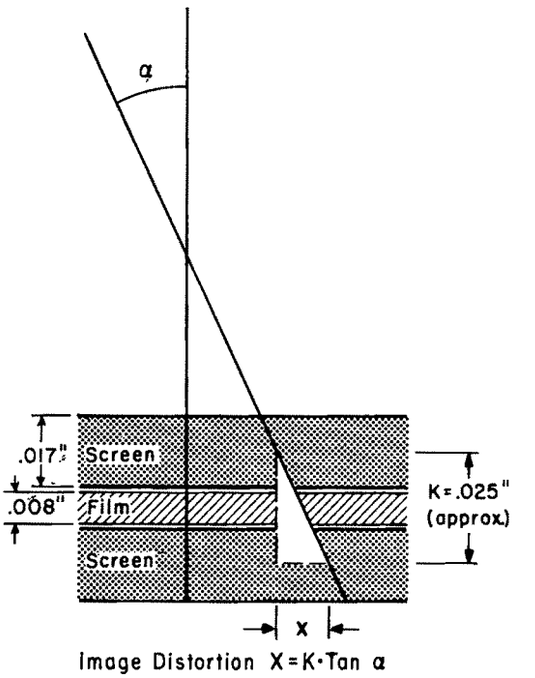


FIG. 15. Image distortion in a double emulsion high speed screen image system.

change in image quality by increasing the depth of the image recording system proves to be below the limits of visibility. It, therefore, seems essential to use double emulsion film in a tomographic system to reduce patient exposure.

SERIES IV. EFFECT OF DOUBLE EMULSION FILM AND SCREENS IN BOTH SYSTEMS

It is more realistic to anticipate a measurable image deterioration from the addition of screens to the image recording system than from the addition of double emulsion film. The image is now recorded in a depth of approximately 0.025 inches, 3 times the depth (0.008 inches) of double emulsion film (Fig. 15). The amount of image deterioration in a screen-film system will become greater as the amplitude of the tomographic movement increases and, in turn, will increase as the level of the fulcrum is raised in an adjustable-fulcrum system. For example, an angle of 45° at the tabletop becomes 57° at a 27 cm. level (Fig. 10).

Screen-film unsharpness will also increase as the object is displaced from the central

TABLE IV

	0°	5°	10°	20°	40°	48°	
Adjustable-fulcrum							Per cent
Phantom— 0 cm. 1.09×	.232	.244	.238	.238	.244		5
Phantom—10 cm. 1.19×	.238	.247	.250	.232	.262		10
Phantom—20 cm. 1.32×	.262	.275	.275	.277	.311		18
Fixed fulcrum							
Phantom at fulcrum—1.33×	.244	.244	.247	.247		.256	5

axis of the system. For compound tomographic movements, film screen unsharpness at any point in the image plane will vary, depending upon the maximal and minimal angles subtended during the blurring movement. Fagerberg[3] has offered a formula ("parallactic blur") to calculate the mean unsharpness in a moving system, but this value can be reasonably appreciated in a static system from the same equation employed to calculate unsharpness in double emulsion film.

The anticipated unsharpness in the central axis of an adjustable-fulcrum tomographic system with double emulsion film and intensifying screens will vary from 0.03 mm. when the fulcrum is at the tabletop and the angle is 5° to 0.36 mm. (12 times as great) when the fulcrum is raised to 27 cm. In a fixed-fulcrum system, the film-screen unsharpness will vary with the angle of section, since there is no angular change with change in focal plane. Maximum variation in a fixed-fulcrum system is from 0.03 mm. at 5° to 0.28 mm. (a factor of 9) at 48°. The same degree of additional unsharpness from lateral displacement of the object from the central axis may be expected.

These concepts may be visually appreciated in the microdensitometric tracings (Fig. 20).

Contrast. A very significant change in contrast takes place in the adjustable-fulcrum system when the fulcrum is raised about the 10 cm. level and the angle is increased beyond 20° (Fig. 16). At the lower level, there is only a 4 per cent decrease in contrast which is essentially the same as was noted in the non-screen systems. At a 10 cm. level, there is a 22 per cent decrease in contrast as the angle of section is increased to 40° and a 26 per cent decrease in contrast is present at the 20 cm. level at 40°. There is only a 6 per cent decrease in contrast as the angle increases from 0° to 48° in the fixed-fulcrum system.

Detail. A proportionate loss of detail occurs as the level of section is raised

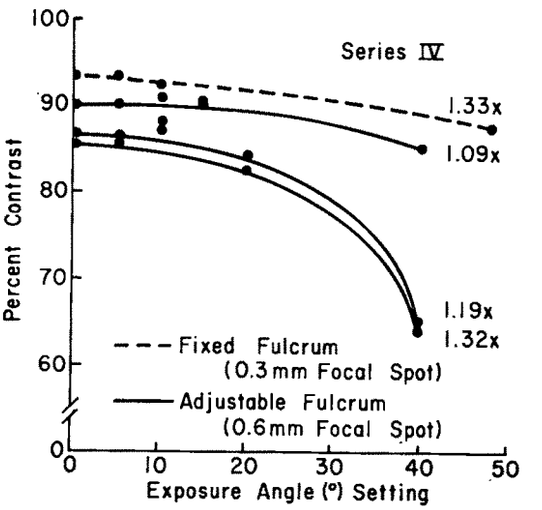


Fig. 16. Effect of double emulsion film and screens on image contrast.

from the tabletop (Table v; Fig. 17). When the fulcrum is at the tabletop, the image diameter with an 0.6 mm. focal spot tube increased 21 per cent as the angle of section increased from 0° to 40°. There is a 41 per cent increase at the 10 cm. level and a 44 per cent increase at the 20 cm. level. The deterioration of resolving power throughout the system, therefore, is equal to a reduction in resolution to 1 line pair/mm.

Diminution in image detail was less in the fixed-fulcrum system showing only a 30 per cent increase in width from 0° to 48°.

When both contrast and detail are considered, the relative degeneration of the image is significantly greater in the adjustable-fulcrum system than it is in the fixed-fulcrum system. Consideration must also be given to the fact that this evaluation only relates to a small object in the central axis of each system.

Series V. Effect of Focal Spot Size on Image Deterioration

Parallel series were done throughout both tomographic systems to determine the effect of focal spot size when screens and double emulsion films were employed. In the fixed-fulcrum system, an 0.3 mm. focal spot tube was used for the fine focus, and a

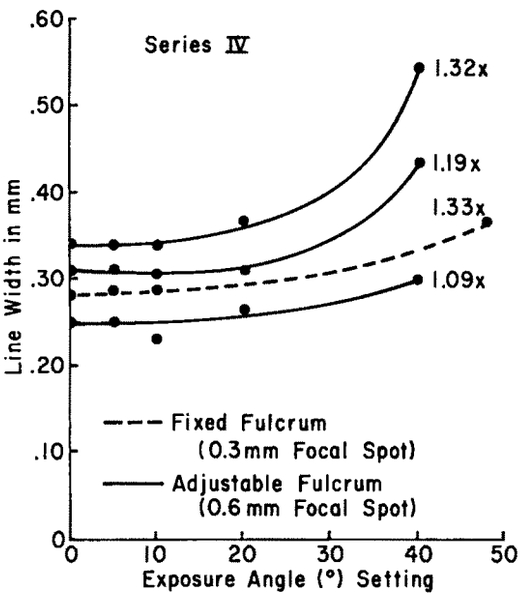


FIG. 17. Effect of double emulsion film and screens on line width.

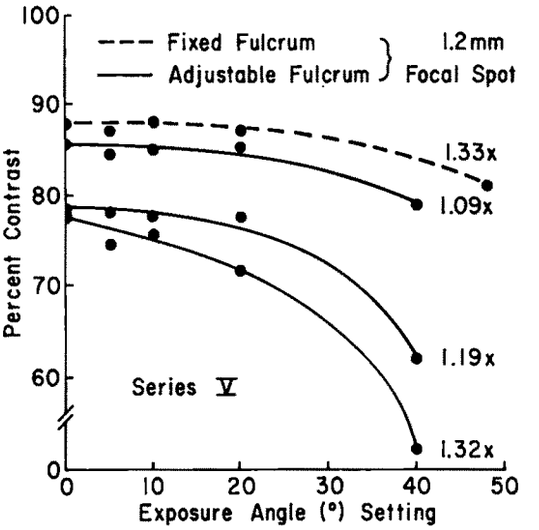


FIG. 18. Effect of focal spot size on contrast (1.2 mm. focal spot).

1.2 mm. focal spot for the large spot. In the adjustable-fulcrum system, an 0.6 mm. focal spot was compared to a 1.2 mm. focal spot.

The results conform closely to those reported by Hale.[4] There is little effect between any of the 3 focal spots employed at low magnification where the small change noted could be accounted for on the basis of distortion. A significant effect was seen with the 1.2 mm. focal spot with wide angles at higher magnification in both systems.

Contrast. The contrast levels were generally lower with the 1.2 mm. focal spot tube (Fig. 18) and, again, the depreciation of contrast was significantly greater in the adjustable-fulcrum system. In the fixed-fulcrum system, only a 6 per cent loss in contrast was noted with both the 0.3 mm. and 1.2 mm. focal spot tubes (Fig. 16; and 18). In the adjustable-fulcrum system, contrast levels were generally lower and proportional decrease of contrast was greater with the 1.2 mm. focal spot tube than it was with the 0.6 mm. focal spot tube. There was a maximum depreciation

TABLE V

	0°	5°	10°	20°	40°	48°	
Adjustable-fulcrum (0.6 mm. fs)	Image diameter in mm.						Per cent
Phantom— 0 cm. 1.09×	.250	.247	.232	.265	.302		21
Phantom—10 cm. 1.19×	.311	.311	.305	.366	.436		41
Phantom—20 cm. 1.32×	.342	.342	.342	.384	.494		44
Fixed-fulcrum (0.3 mm. fs)							
Phantom at fulcrum—1.33×	.280	.293	.290	.311		.366	30

TABLE VI

CHANGE IN IMAGE DIAMETER WITH 1.2 MM. FOCAL SPOT

	0°	5°	10°	20°	40°	48°	
Adjustable fulcrum (1.2 mm. fs)	Image diameter in mm.						Per cent
Phantom— 0 cm. 1.09×	.287	.293	.287	.305	.342		19
Phantom—10 cm. 1.19×	.378	.378	.378	.378	.470		24
Phantom—20 cm. 1.32×	.506	.500	.458	.537	.610		21
Fixed-fulcrum (1.2 mm. fs)							
Phantom at fulcrum—1.33×	.366	.397	.397	.415		.488	33

of 26 per cent with a large focal spot at 1.32× magnification.

Detail. The change of image diameter with the small focal spot can be noted in Table v and Figure 17, and is to be compared to the image diameters produced with the large focal spots (1.2 mm.) in Table vi and Figure 19.

It was not possible to make a comparison between the 2 fine focus tubes (0.3 mm. and 0.6 mm.) because of the different geometries in the 2 systems. A very distinct change in image diameter is noted between the small and large focal spots employed, with significantly greater deterioration in the adjustable-fulcrum system from a base image diameter (1.09× magnification) of .287 mm. increasing to .610 mm. at 1.32× magnification (Table vi). This magnitude of change will significantly affect the resolution of the system. Image width in the fixed-fulcrum system with a large focal spot is almost identical with that noted at the 10 cm. level (1.19×) in the adjustable-fulcrum system (Fig. 19). A visual appreciation of these changes is noted in Figure 20.

The deterioration resulting from a change in focal spot size, therefore, is proportionately greater in the adjustable-fulcrum system, showing significant deterioration from a base image which could be expected to resolve 2 line pairs to an image which would exhibit a resolving power of less than 1 line pair/mm.

Another aspect of focal spot size is worthy of consideration at this point. If the focal spot is larger than the object, there will be a decrease in the size of the principal image of the object to a point where it disappears. The magnitude of this change depends upon the focal spot size and the object size. Figure 21 indicates the change in size of the principal image when the focal spot is 2×, 1× and 0.5× the size of the object. When the object is smaller than the focal spot (Fig. 21A), the prin-

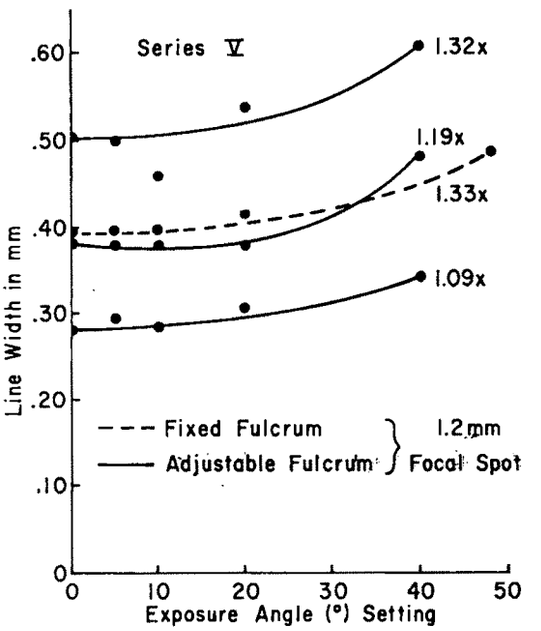


FIG. 19. Effect of focal spot size on image width (1.2 mm. focal spot).

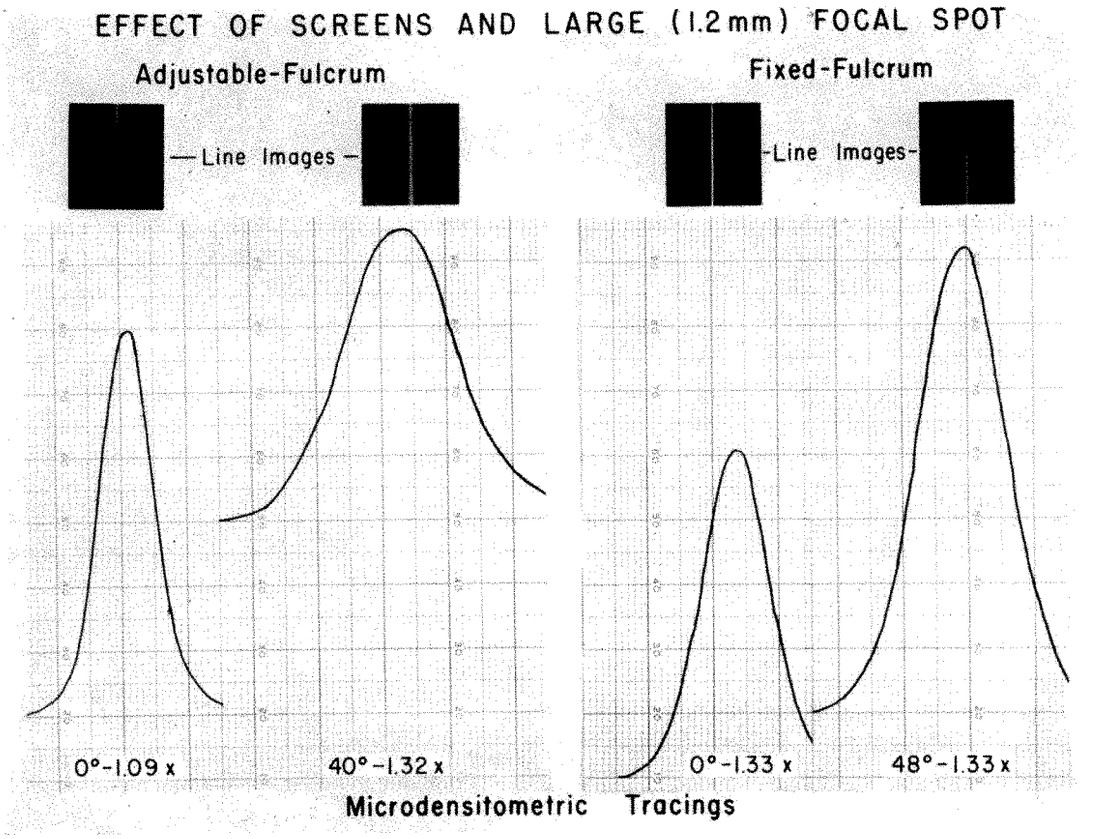


FIG. 20. Effect of screens and large focal spot (1.2 mm.) on line image in both systems. Note marked deterioration of image in the adjustable-fulcrum system at the 20 cm. level (1.32× magnification).

cipal image is smaller than the object and its zone of unsharpness is proportionately larger. When the focal spot and object are the same size (Fig. 21B), the principal image is the same size as the object and the zone of unsharpness becomes smaller. As the focal spot becomes smaller than the object (Fig. 21C), the magnification increases and the zone of unsharpness becomes proportionately smaller so that we are now approaching the optimal situation of a point source.

The uniformity of the focal spot is a consideration. Non-uniformity of the focal spot will alter these geometric considerations. There will also be a difference of the effective focal spot for objects on the anode side of the tube as opposed to the cathode side.

It may be generally stated, however, that it is advantageous to employ the smallest focal spot practical in any tomographic system.

SERIES VI. A COMPARISON OF EIGHT DIFFERENT SCREENS

(Examined at low kilovoltage)

In an effort to use the optimal screen in the film-screen systems, 8 commercially available intensifying screens were examined as follows: DuPont Detail; DuPont Par Speed; DuPont Hi-Speed; DuPont Hi-Plus; Radelin Par Speed (T-2); ERKA-Rapid; CAWO-Special; and Philips Ultra-S.

All screens were examined in the fixed-fulcrum system with the object at the fulcrum and the screen in the Bucky tray. Exposures were made at 45 kv. and 40 ma., adjusting the time to equalize the base

density of the film. The DuPont Hi-Plus screen gave the best compromise of contrast and detail with the least amount of radiation (3.2 mas.).

SERIES VII. EFFECT OF LOW *VERSUS* HIGH MILLIAMPERAGE

An attempt was made to determine any possible change between low and high milliamperage ranges. Films were exposed in the fixed-fulcrum system employing an 0.3 mm. focal spot tube with double emulsion film and screens. No significant change in image diameter was noted between low and high milliamperage, although the range of milliamperage was relatively small (Table VII).

SERIES VIII. EFFECT OF TUBE TEMPERATURE

Image diameter was examined with the first exposure of the tube in the morning at which time the tube temperature was considered to be at a base level. A second exposure of the phantom was made immediately following the completion of a long series of tomographic exposures, employing high milliamperage. Only minor change in image diameter is noted between a cold and hot tube (Table VIII).

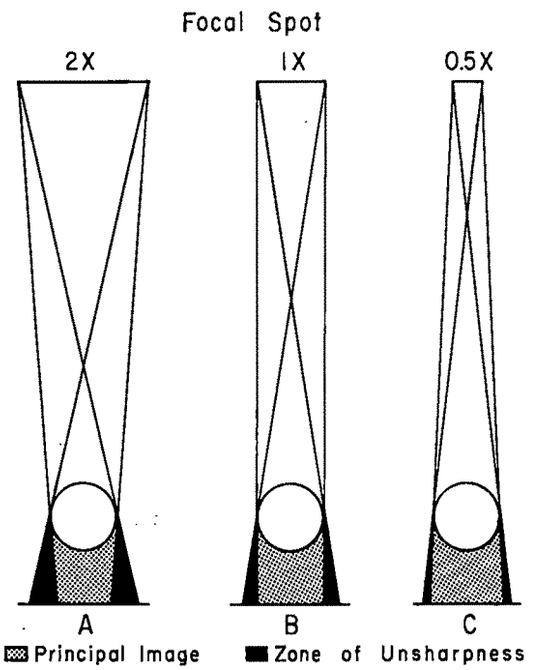


FIG. 21. Drawing to illustrate change in image size with change in size of focal spot.

TABLE VII

EFFECT OF MILLIAMPERAGE CHANGE ON IMAGE SIZE

	Image diameter in mm.	
	0°	48°
Low milliamperage (4 ma.)	.241	.250
High milliamperage (40 ma.)	.256	.256

TABLE VIII

EFFECT OF TUBE TEMPERATURE ON IMAGE SIZE

	Image diameter in mm.
	0°
Cold tube	.244
Hot tube	.250

SERIES IX. EFFECT OF SCREEN TEMPERATURE

A 25 per cent change in image diameter was noted when the temperature of the intensifying screens was changed from 95°F. to 17°F. (Table IX), the image width being greater at 95°F.

There is, therefore, no significant effect of changing from 4 ma. to 40 ma. and no appreciable image deterioration noted between a hot and a cold x-ray tube employing the same focal spot. Screen tempera-

TABLE IX

EFFECT OF SCREEN TEMPERATURE ON IMAGE SIZE

	Image diameter in mm.
Screen temperature	0°
17° F.	.224
75° F.	.268
95° F.	.305

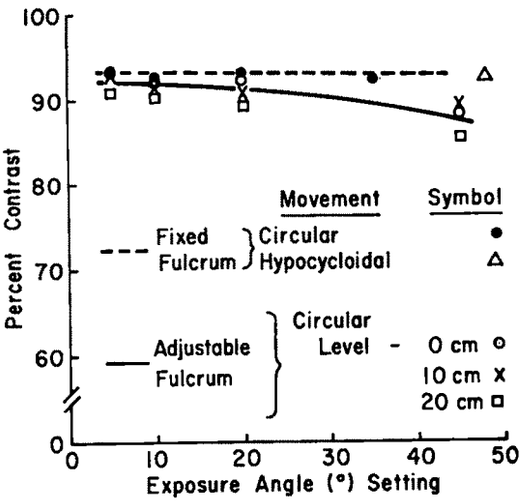


FIG. 22. Contrast changes in the tomograms.

ture, however, does appear to have a definite effect with better image quality at lower temperatures. This latter finding merits further investigation with different screens and different kilovoltage levels.

SERIES X. THE TOMOGRAMS

Contrast. In general, the same type of image deterioration noted in the static systems could be detected in the tomograms. Contrast levels of the tomograms in general were lower in the adjustable-fulcrum system and showed the same type of decrease in contrast when wide angles were employed, as was noted in the static system. There was no significant change in contrast throughout the tomograms made in the fixed-fulcrum system. Contrast levels in the central portion of the tomogram of the fixed-fulcrum system showed no significant variation between the 5°, 10°, 20° and 36° circular and hypocycloidal movements (Fig. 22).

Detail. The width of the image increased disproportionately in the adjustable-fulcrum system as the fulcrum was raised from the tabletop to a level of 20 cm. Again, the change was greatest with the movements employing wide angles. Figure 23 shows the change in image width as a 45° circle is elevated from 0 to 20 cm. No significant change in image width was noted throughout the fixed-fulcrum system. The hypocycloidal movement compared favorably with the trispiraled movement at a 10 cm. level. The trispiraled movement made with a higher fulcrum level showed a generally wider image as noted in Figure 23.

GRID EFFECT

It must also be considered that image degeneration for objects in lateral positions of the image field will experience disproportionately greater deterioration in the adjustable-fulcrum system than in the fixed-fulcrum system because of increased grid cut-off as the layer heights are changed from tabletop to 27 cm. The grid in an adjustable-fulcrum system is focused from the film level or 120 cm., to accommodate conventional radiography. As the level of section is raised and the angle increased, the focus-grid distance increases from 120 cm. to 136.4 cm. for objects in the central axis of the field (Fig. 10). The loss of primary radiation from far-focus-grid decentering (Fig. 24) can be calculated from the following formula (Christensen[2]):

$$L = rc\left(\frac{1}{f_0} - \frac{1}{f_2}\right) \times 100,$$

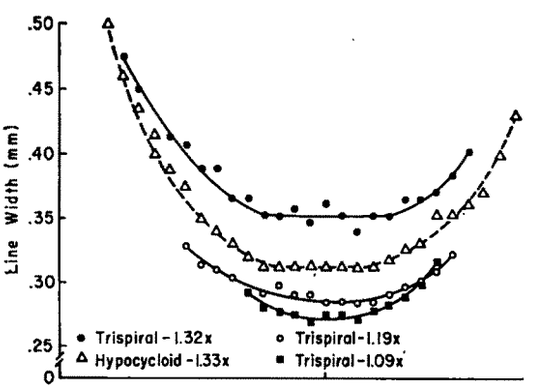


FIG. 23. Charting of line width of multiple microdensitometric tracings across a tomographic image of the wire. The line widths at half maximum are plotted. Note the uniformity of the image with the hypocycloidal movement in the fixed-fulcrum system.

TABLE X

LOSS OF PRIMARY RADIATION (PER CENT) FROM FAR-FOCUS-GRID DECENTERING
(Adjustable-fulcrum system at 45°)

		Lateral Deviation in Inches							
		1	2	3	4	5	6	7	8
Adjustable-fulcrum	10 cm.	1.2	2.3	3.6	4.8	6.0	7.2	8.4	9.6
Grid Focus—120 cm.	27 cm.	2.64	5.28	7.92	10.56	13.20	15.84	18.48	

where L = loss of primary radiation (%), r = grid ratio, f_0 = grid-focusing distance, f_2 = target-grid distance, and c = distance from center of grid.

Loss of primary radiation (%) from far-focus-decentering in an adjustable-fulcrum system with a grid having a 12:1 ratio can be appreciated from Table x.

The loss of primary radiation from lateral decentering may be very significant, although it is still less in the fixed-fulcrum system even with grids of comparable ratio (Table xi). Caution should be exercised in the proper selection and alignment of focused grids in any tomographic system.

DISCUSSION

It may be reasonably concluded, therefore, that the use of intensifying screens in tomographic procedures is essential because of exposure factors. Even when optimal screens are selected, significant image deterioration occurs as the result of the increase in depth of the image recording system and grain of the screen. Both contrast and detail diminish as magnification and angle of section increase in an adjustable-fulcrum system. Greatest change occurs at higher levels and wider angles. In general, deterioration becomes accelerated at levels above 10 cm. and at angles greater than 20°. The change in contrast is not significant in the fixed-fulcrum system and change in image detail is approximated by the loss of detail noted at a 10 cm. level in the adjustable-fulcrum system.

Further deterioration of the image, particularly of image objects in the lateral field, can be expected from inherent far-focus-grid decentering in an adjustable-fulcrum system when up to 10 per cent of the primary radiation will be lost with grid cut-off in the lateral fields. Since only the central portion of the field was examined in this exercise, no appreciable grid cut-off was noted (Fig. 24). Lateral-focus-grid decentering is more significant and can lead to 100 per cent loss of primary radiation at a 4 inch lateral position with a 12:1 grid in the adjustable-fulcrum system and a 100 per cent loss at a 5 inch lateral position in a fixed-fulcrum system (Table xi).

SUMMARY

A microdensitometric study of image quality appears to lend itself satisfactorily to the examination of tomographic images. Multiple films of a standard phantom, con-

TABLE XI

LOSS OF PRIMARY RADIATION WITH LATERAL DEVIATION

	1	2	3	4	5
Fixed-fulcrum (56 inches)	21.4	42.9	64.3	85.7	100
Adjustable-fulcrum (47½ inches—12: 1 grid)	25.4	50.8	76.2	100	

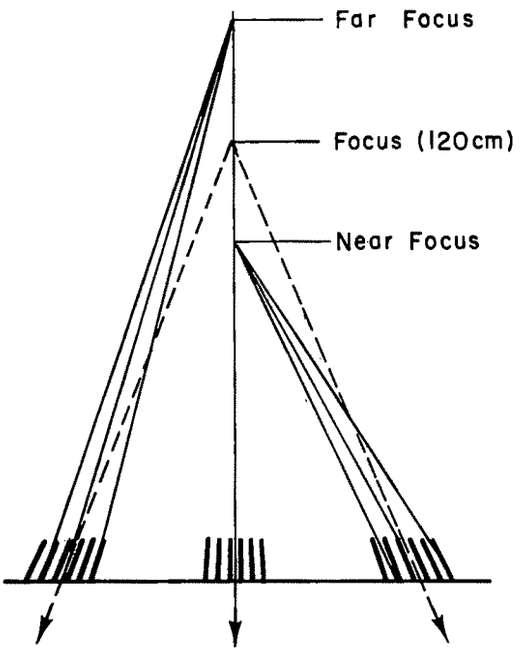


FIG. 24. Further deterioration of the image, particularly of image objects in the lateral field, can be expected from inherent far-focus-grid decentering in an adjustable-fulcrum system when up to 10 per cent of the primary radiation may be lost with grid cut-off in the lateral fields. Since only the central portion of the field is examined in this exercise, no appreciable grid cut-off is noted.

sisting of a strand of 0.254 mm. polished tungsten wire, were exposed throughout the variable geometries of an adjustable-fulcrum tomographic system and a fixed-fulcrum tomographic system. The following general conclusions may be drawn:

1. There is a minimal change in image quality between single emulsion and double emulsion film. These change are below the limits of visibility in the roentgenogram.

2. The addition of intensifying screens produces a significant deterioration of the image throughout both systems. The deterioration is greater in the adjustable-fulcrum system and becomes more pronounced as the layer height is elevated above the tabletop and the angle of section is increased. Image deterioration at levels above 10 cm. and with angles greater than 40° are very substantial, leading to significant loss of contrast and increase in image width by magnification and distortion.

There is little change in contrast levels throughout the fixed-fulcrum system and, again, there is only minimal magnification and distortion.

It is important, therefore, that careful attention be given to the selection of optimal screens in any tomographic system. Image quality will decrease disproportionately throughout the tomographic system when poor screen performance is employed.

3. Image quality is inversely proportional to the size of the focal spot used. It was not possible to draw any specific conclusions between the image quality resulting from the use of an 0.3 mm. tube as compared with an 0.6 mm. tube. There was, however, very significant difference between the small focal spots and the large 1.2 mm. focal spots in both systems. The effect of the large focal spot is, again, disproportionately greater in the adjustable-fulcrum system. It is, therefore, important to use the smallest practical focal spot in any tomographic system.

4. No significant effect was noted in image quality as the result of milliamperage change or whether the tube was cold or at a high temperature level. A very definite effect of image quality was noted when the screen temperature was changed from 17° F. to 95° F. There was significant degeneration of the image at a screen temperature of 95° F. This finding should be investigated more completely with variable screens and beam qualities. It is conceivable that the routine use of low temperature screens would improve the screen performance and ultimately reduce patient exposure.

5. There is inherent far-focus-grid decentering in an adjustable-fulcrum tomographic system. The effect of this type of grid decentering is not significant in the central axis of the tomographic system, but it does become reasonably significant near the periphery of a large image field. The

addition of any lateral-grid decentering compounds this effect. Proper grid selection is important in any tomographic system and perhaps a 10:1 ratio grid would be more satisfactory in a tomographic system than a 12:1 ratio grid. The grid in a fixed-fulcrum system is not liable to far-focus-grid decentering and a lateral-focus decentering becomes less significant in the fixed-fulcrum system.

6. DuPont Hi-Plus screens gave the best image quality of this phantom from 8 screens examined and showed better retention of image quality than the other high speed screens. These films were exposed at low kilovoltage levels and this conclusion may not be valid at higher energy levels.

7. Image quality changes noted within the static system are reflected directly in the same proportion in the tomograms. A general deterioration of the image, both in contrast and detail, is noted throughout the adjustable-fulcrum system as the result of increased magnification and distortion and it becomes disproportionately greater for objects displaced from the central axis of the system. Both contrast and image quality are more uniformly maintained throughout a fixed-fulcrum system.

8. Manufacturers are urged to give consideration to these findings in the development of future tomographic devices.

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The authors wish to gratefully acknowledge the generous cooperation of the officials and scientists, especially Drs. Holland and Williams, of the Eugene Sullivan Laboratory, Corning Glass Works, Corning, New York, for placing a suitable microdensitometer* at our disposal. This study would not have been possible without their assistance.

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* Jarrell-Ash microdensitometer with slit dimensions: 57.1 × 1143 microns.

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EDITORIALS

THE INTER-AMERICAN COLLEGE OF RADIOLOGY

THE Inter-American College of Radiology becomes 30 years of age in 1973. The objective of the College has been to associate the radiologists of the Western Hemisphere in a professional organization, with representatives in all countries of the New World, in order to:

1. promote progress in the practice of radiology
2. protect the rights and privileges of radiologists in their respective countries
3. facilitate scientific interchange among its members through national and inter-american conferences
4. institute programs of training for young radiologists
5. support research in this medical specialty
6. publish a regular periodical as a medium for scientific contributions.

The Inter-American College has held 10 congresses; the last one took place in San Juan, Puerto Rico, in May, 1971; the Eleventh Inter-American Congress of Radiology will take place in Bogotá, Colombia, in 1975. The College has published a quarterly, *Revista Interamericana de Radiología* which has been distributed to its members for many years. At present the College is dedicating its efforts to the development of national seminars with Inter-American participation; the College has just announced also the creation of three annual prizes (see Feb. 1973, p. 465) to stimulate research and original publications in radiodiagnosis, radiotherapy, and nuclear radiology. The College was not founded as a federation of national societies; we are now seeking support of national radiological societies towards a greater continental unity in the profession. Anticipating the Congress of 1975, efforts are being made to secure facilities to College members (leaves of absence, currency exchange, etc.) to make it possible for radiologists to attend.

We urge radiologists in all countries of the Americas to consider the efforts of the College as a genuine manifestation of hemispheric solidarity and fraternity. The College is in need of your moral support. But all of us are in need of better understanding that will bring us greater harmony. Common efforts have brought a remarkable degree of progress in the past; continued progress and productivity are possible.

We wish to issue a fraternal appeal to all radiologists in the Americas to join us to achieve these aims. If he is not already known to you, we will be glad to send you the name and address of your national Councillor, through whom your application for membership can be initiated.

MIGUEL DAO, M.D., *President*
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SI UNITS IN RADIOLOGY AND RADIATION MEASUREMENT

AFTER a considerable time of preparatory work, the International Commission on Radiation Units and Measurements (ICRU) in 1953 to 1962 presented its definitions of the quantities absorbed dose, exposure and activity and the corresponding special units 1 rad, 1 röntgen (1 R) and 1 curie (1 Ci). They are now generally accepted in the whole field of radiology and radiation protection for routine use, although certain misuse of some of these quantities is still noticed.

Simultaneously with the work of the ICRU, international efforts were going on in order to establish a practical system of units of measurement suitable for adoption by all signatories to the Metre Convention. In 1960 the 11th General Conference of Weights and Measures (CGPM) adopted the International System of Units, with the international abbreviation SI, for this practical system. Today SI is officially introduced in a large number of countries, including the USSR and the member countries of the European Economic Community (EEC). A remarkable exception is the USA.

It is clear that the general implementation of SI means new difficulties in the future use of the special radiological units. When they were introduced in the 1950s, a fully developed SI system was not available. Nevertheless, the units curie, röntgen and rad can all be exactly expressed in SI units in the following way:

$$1 \text{ curie} = 1 \text{ Ci} = 3.7 \times 10^{10} \text{s}^{-1} \text{ (exactly)}$$

$$1 \text{ röntgen} = 1 \text{ R} = 2.58 \times 10^{-4} \text{C} \cdot \text{kg}^{-1} \text{ (exactly)}$$

$$1 \text{ rad} = (1 \text{ rd}) = 0.01 \text{ J} \cdot \text{kg}^{-1} \text{ (exactly)}$$

It follows from the strict SI rules that the numerical factors involved prevent the adoption of these units as SI derived units. However, in view of existing practice, the International Committee of Weights and Measures (CIPM, 1969) considered it was preferable to keep the units curie, röntgen and rad *for the time being*, to be used with the SI. But steps towards the eventual abandonment of the special radiological units have already been taken by the EEC countries. And the important benefits to be gained by worldwide use of a common international and coherent system of quantities and units now calls upon a careful consideration of the "be or not to be" of the special radiological units.

Radiological SI units and their equivalents expressed in the present special units are given in Table 1. This table shows that the SI units imply substantial changes in the numerical values of the actual quantities. In the case of an *absorbed dose* of 6,400 rad to a patient, a change to the corresponding SI quantity value 64 J/kg should be relatively easy to perform. The difficulties may be more pronounced if the absorbed dose rate has to be expressed in watts per kilogram, W/kg, replacing rad/min, because the time unit is not explicitly given in the unit W/kg, which also masks the fact that the time unit is the second and not the minute. From a medical safety point of view it is also desirable that the absorbed dose and absorbed dose rate be expressed in units containing the same derived SI unit. The units J/kg and J/(kg·s) should then be the better choice; even J/(kg·min) for absorbed dose rate could be considered, as minute is retained for general use with the SI units.

The quantity *exposure* will be given a rather large SI unit, 1 C/kg, and an inconvenient conversion factor, 1 C/kg ≈ 3,876 R. The main field for the use of the quantity exposure will be medical roentgen diagnosis. For instance, the exposure rate 20 R/s corresponds to 0.0052 C/(kg·s) *or* 5.2 mC/(kg·s) *or* 5.2 mA/kg; a 10 mR film exposure equals 2.6 μC/kg. This change to

TABLE I

RADIOLOGICAL SI UNITS

Quantity	Derived SI Unit	Symbol	Present Equivalent
Activity	1 per second	s^{-1}	$\approx 2.703 \times 10^{-11}$ Ci
Absorbed dose	1 joule per kilogram	$J \cdot kg^{-1}$	100 rad
Absorbed dose rate	1 watt per kilogram	$W \cdot kg^{-1} = J \cdot kg^{-1} \cdot s^{-1}$	100 rad $\cdot s^{-1}$
Exposure	1 coulomb per kilogram	$C \cdot kg^{-1}$	$\approx 3{,}876$ R
Exposure rate	1 ampere per kilogram	$A \cdot kg^{-1} = C \cdot kg^{-1} \cdot s^{-1}$	$\approx 3{,}876$ R $\cdot s^{-1}$

an SI unit may involve some difficulties for persons with insufficient experience in handling the results of physical measurement.

The replacement of the *activity* unit 1 curie with the SI unit 1 per second, s^{-1}, seems to imply certain particular problems. The SI unit is inconveniently small (Table 1) and the formation of the necessary multiple units will not be possible in the usual straightforward way. For instance, the activity 10^6 s^{-1} (≈ 27 μCi) can *not* be written Ms^{-1}, as, according to the strict SI rules, this means $(Ms)^{-1}$ or 1/Ms, which is equal to 10^{-6} s^{-1}. The recommended symbol for 10^6 s^{-1} is then 1 μs^{-1}, one per microsecond; for 10^9 s^{-1} (≈ 27 mCi) it is 1 ns^{-1}, one per nanosecond, etc. And the rate of change of a radioactive substance necessitates the use of notations such as 10 per microsecond per second, 10 $\mu s^{-1}/s$. Both examples may create confusion and increased risk of mistakes in radiation protection operations and in clinical practice.

The safety of the patient in medicine and hospital care has to be carefully considered before the responsible national authorities prescribe a change in the present system of units. A replacement of the special radiological units with SI units implies several difficulties, as shown by the examples above. Some of these problems may well be solved by introducing new names for the derived SI units discussed in this context. However, such new names are not desirable according to the principles of the CGPM; nevertheless, this body recently accepted special names for the unit of pressure (1 pascal) and of electric conductance (1 siemens). Other measures may also be suggested in order to overcome the difficulties.

The International Commission on Radiation Units and Measurements (ICRU) has as its principal objective the development of internationally acceptable recommendations regarding quantities, units and measurement of ionizing radiation and radioactivity. The ICRU therefore invites and welcomes constructive comments and suggestions regarding the possible replacement of the special radiological units 1 rad, 1 röntgen and 1 curie with derived SI units. These comments may be transmitted to the Chairman, Dr. H. O. Wyckoff,* the Vice Chairman Professor A. Allisy,† or the present writer.

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EVERETT E. SEEDORF, M.D.
1905–1973

DR. EVERETT E. SEEDORF, born in 1905, died on January 4, 1973 as the result of metastatic carcinoma of the lung.

He received his premedical education at the University of Illinois, graduating in 1930, and received his M.D. degree from the University of Wisconsin in 1936. That same year he married Annette L. Lloyd.

His Internship was served at the Milwaukee Hospital, Milwaukee, Wisconsin, and his training in Radiology was at the Mayo Clinic, Rochester, Minnesota. He received the M.A. Degree in Radiology from the University of Minnesota in 1940. He

was certified by the American Board of Radiology that same year.

He served on the staff at the St. Francis Hospital, LaCrosse, Wisconsin, from 1940 to 1945, and also served on the staff at St. Mary's Hospital, Sparta, Wisconsin, from 1943 to 1945.

From 1945 to 1955 he served on the staff of the Scott and White Clinic, Temple, Texas. During this same period he was on the staff of the Santa Fe Hospital, Temple, Texas. During this period he was an Associate Professor of Radiology of the University of Texas Post-Graduate School of Medicine.

In 1949 he received a Gold Medal from the American Medical Association for his exhibit on the study of colon carcinoma.

From 1955 until 1973 he served on the staffs of the Pekin Memorial Hospital, Pekin, Illinois, and the Proctor Community Hospital, Peoria, Illinois.

Dr. Seedorf became a member of the American Roentgen Ray Society in 1947 and a Fellow in the American College of Radiology in 1950.

He is survived by his wife, a son, Richard, three daughters, Ellen, Sally, and Donna, and seven grandchildren.

Dr. Seedorf will be long remembered by his colleagues and patients for his boundless energy, and his love of life, his family, and his church. His pleasant personality and kindness were unexcelled. He will be sorely missed by his colleagues, patients, family, and friends.

Robert L. Tucker, M.D.

Hansen-Seedorf Radiological Group,
Peoria, Illinois

NEWS ITEMS

CURRENT TECHNIQUES IN RADIATION THERAPY

External Beam: Part II

The Department of Therapeutic Radiology and the Office of Postgraduate Medical Education of the University of Minnesota announces the above course, to be held at the Mayo Memorial Auditorium, May 16–18, 1973.

This course is designed primarily for general radiologists, therapeutic radiologists, and residents. It will present practical concepts in radiation treatment utilizing external beam to include techniques in cervix, vagina, endometrium, ovary, and other gynecologic cancers, bladder, prostate, testicle, colo-rectal cancers, non-Hodgkin's lymphomas, and bronchogenic cancer. Also included will be a clinically oriented analysis of the various external beam supervoltage units, their practical applications and relations to basic treatment patterns. There will also be demonstrations of brachytherapy, applications and a discussion of the practical applications of the computer, and combined chemotherapy and radiation therapy in the treatment of solid tumors in adults.

The Director is Dr. Seymour H. Levitt, Professor and Head, Department of Therapeutic Radiology, University of Minnesota Medical School.

The distinguished Guest Faculty includes: Malcolm A. Bagshaw, Stanford; Luther W. Brady, Philadelphia; Luis Delclos, Houston; Gilbert H. Fletcher, Houston; Morton M. Kligerman, Albuquerque; Fearghus O'Foghludha, Durham; Vera M. Peters, Toronto; William E. Powers, St. Louis; Vincent Sampiere, Houston; Norah duV. Tapley, Houston; Taylor Wharton, Houston; and Morris J. Wizenberg, Baltimore. The remainder of the faculty will include members of the teaching staff of the University of Minnesota Medical School and the Mayo Graduate School of Medicine.

FIFTEENTH ANNUAL REFRESHER COURSE IN DIAGNOSTIC ROENTGENOLOGY

University of Cincinnati Medical Center

The "Fifteenth Annual Refresher Course in Diagnostic Roentgenology" will be held by the Radiology Department of the University of Cincinnati College of Medicine, under the direction of Dr. Benjamin Felson, May 29–June 2, 1973.

The course will include, in addition to lectures and demonstrations, teaching methods employing audience participation.

Saturday, June 2, will be devoted entirely to radiation physics.

Because of limited seating capacity, applicants will be accepted in order of receipt of inquiries.

Further information concerning the course, which is open to radiologists and radiology residents, may be obtained by writing to Dr. Harold B. Spitz, Department of Radiology, Cincinnati General Hospital, Cincinnati, Ohio 45229.

A POSTGRADUATE COURSE IN RADIATION BIOPHYSICS

Columbia University College of Physicians and Surgeons

This course is planned for Physicists, Medical Physicists, Radiotherapists and Radiation Biologists under the direction of Eric J. Hall, Ph.D., and will be held June 26–29, 1973.

The course is designed to impart knowledge in the areas of dosimetry, microdosimetry, radiobiology and radiobiologic theory. Topics of special emphasis will be radiation therapy with high LET radiation, and experimental radiobiology with special emphasis on RBE and OER.

A knowledge of the basic physics and biology relevant to radiotherapy will be required, but students having little proficiency in one of these areas will have an opportunity to attend one of two parallel introductory sessions on these subjects which will be given on the first day.

The visiting Faculty consists of Dr. J. Brennan, University of Pennsylvania and Dr. H. D. Suit, Harvard University.

The College Faculty includes: Dr. V. P. Bond; Dr. W. Gross; Dr. E. J. Hall; Dr. A. M. Kellerer; and Dr. H. H. Rossi.

For further information, please write to Dr. Melvin D. Yahr, College of Physicians and Surgeons, Columbia University, 630 W. 168th Street, New York, N. Y. 10032.

SYMPOSIUM ON POLYTOMOGRAPHY OF THE TEMPORAL BONE

The 7th two day "Symposium on Polytomography of the Temporal Bone" will be given under the auspices of The Wright Institute of Otology at Community Hospital, Indianapolis, Indiana, on June 2 and 3, 1973.

The subjects covered are: Basic Anatomy of the Temporal Bone; and Technique of Polytomography of the Temporal Bone, with demonstrations of normal tomograms. Pathologic conditions revealed by polytomography, such as cholesteatoma, ossicular chain problems, otosclerosis, fractures, foreign bodies, tumors, and congenital anomalies will be shown on original tomograms and the clinical applications discussed.

The number of registrants is limited to 18.

Inquiries should be directed to: The Wright Institute of Otology, Inc., Community Hospital of Indianapolis, Inc., 1500 North Ritter Avenue, Indianapolis, Indiana 46219.

PHYSICAL ASPECTS OF NUCLEAR MEDICINE

A special summer program will be given at M.I.T., July 23–27, 1973.

This Special Summer Program will deal with the state of the art in physical problems related to nuclear medicine. Special emphasis will be placed on instrumentation, radiopharmaceuticals, dosimetry and data processing as well as specific organ studies and therapy.

The material should be of value to both physicians and physical scientists working in this area.

The Program is jointly sponsored by the Harvard Medical School and M.I.T. through the Harvard-M.I.T. Program in Health Sciences and Technology. Some tuition grants will be available.

For further information, please write to: Director of the Summer Session, Room E19-356, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139.

RECENT ADVANCES IN NUCLEAR MEDICINE

A course on "Recent Advances in Nuclear Medicine" will be held August 20–24, 1973 at Colby College in Waterville, Maine.

For the fifth consecutive year, the course will be given by the Division of Nuclear Medicine of the Johns Hopkins Medical Institutions under the direction of Dr. Henry N. Wagner, Jr.

This year, advances in the broad field of Nuclear Medicine, as well as in-depth discussions of basic principles will be presented. In particular, *in vitro* procedures, clinical imaging procedures, and newer aspects of instrumentation will be emphasized.

For further information, please contact Dr. Robert Kany, Director of Special Programs, Colby College, Waterville, Maine 04901.

FIFTH INTERNATIONAL CONGRESS OF RADIATION RESEARCH

In the November 1972 issue of this JOURNAL (p. 690), a preliminary announcement was made of the fifth quadrennial meeting of the International Association of Radiation Research (IARR), which is to be held in Seattle, Washington, U.S.A., July 14–20, 1974.

President V. P. Bond takes distinct pleasure, on behalf of the International Association for Radiation Research, the Radiation Research Society of America, and the Officers and members of the Organizing Committee of the present Congress, to extend a special invitation to colleagues from all parts of the world to attend the Fifth International Congress of Radiation Research.

President Bond informs us that the First International Congress of Radiation Research was held in Burlington, Vermont in 1958, followed by Congresses in England, Italy, and France, in 1962, 1966, and 1970, respectively. All of these international meetings provided excellent milieu for the exchange of new ideas in radiation research. The present Congress has every promise of continuing this tradition of scientific excellence.

In addition, the incomparable beauty of the setting in Seattle should make this a memorable experience for all. The scientific sessions and other activities of the Congress will be held in the Seattle Center, a large park-like area in the heart of Seattle. The Center has excellent meeting facilities and a variety of restaurant facilities; it is readily accessible to downtown Seattle via a 90 second monorail ride.

The Plenary Sessions have as subjects:
The future of power sources—implications for man and his environment.
Physical, radiobiological, and radiotherapeutic aspects of heavy ions and neutrons.
Re-evaluation of present limits for radiation exposure in view of the effects of environmental agents other than radiation.

The symposia topics include: repair of genetic damage; radiocarcinogenesis; dose rate effects in mammalian cells; radiation mutagenesis; biochemical aspects of repair; nature of radiation target in repair proficient cells; radiotherapy (cellular repair, repopulation, redistribution in the cell cycle, reoxygenation, time dose relationships, low dose rate irradiation, etc.); biological action of heavy ions; theoretical models; solvent dependence of spectra; dynamics of solvation; kinetics of geminate pair decay; initial electron yields; electrons in hydrocarbons and non-polar liquids; electrons in aqueous systems; excited states in radiation chemistry; internal emitters; late effects of radiation—life shortening; radiation ecology; radiation biology of slowly renewing tissues; agricultural radiation biology; radiostimulation; species variation in radiosensitivity; normal tissue injury; cell transformation; radiation related environmental topics; application of radiation methods for the study of electron transfer reactions; radiation methods in the study of the structure of liquids; application of pulse radiolysis and other fast response techniques to molecular radiation biology; cellular radiation sensitization.

In the past, the IARR has accepted as official languages of the Congress, English and the language of the host country. Since this Congress will be held in the United States, the IARR decided at Évian in 1970 that the official language will be English only.

The deadline for hotel reservations, registration, and abstracts is likely to be February 1, 1974, but earlier registration will be helpful to the Congress organizers. Earlier hotel reservations are more likely to ensure the type of accommodations desired.

The second brochure, together with registration forms, hotel reservation forms, etc., will be mailed by the Secretary-General about September, 1973. To ensure receipt of this brochure, please contact W. K. Sinclair, Secretary-General, 5th International Congress of Radiation Research, Argonne National Laboratory, Argonne, Illinois 60439.

BOOK REVIEW

Technique of Lymphography and Principles of Interpretation. By Hans Kuisk, M.D., D.Sc., Assistant Professor of Radiology, College of Medical Sciences, University of Minnesota; Chief, Radiation Therapy, Radiology Service, Veterans Administration Hospital, Minneapolis, Minn.; Formerly, Chief Assistant, Institute of Microbiology, University of Tartu, Estonia. Cloth. Pp. 320, with many illustrations. Price, $22.50. Warren H. Green, Inc., 10 South Brentwood Boulevard, St. Louis, Mo. 63105, 1971.

The need for a concise, complete and easily understandable work on lymphography has been admirably satisfied by Dr. Kuisk's book. In a relatively few pages he has managed to cover the history of the procedure, its techniques and complications, and its various applications in a host of disease entities where useful information may be obtained by this means.

The novice may find the sections on interpretation very limited and disappointing in the lack of definitive differential information. This may reflect the relatively limited experience with lymphography in some of these diseases and perhaps also the limitations of the procedure itself.

This book is amply illustrated with good correlation between the text and the illustrations. The illustrations are of fairly good quality and demonstrate the author's points to good advantage. The bibliography is adequate.

I believe that this work should be part of the library of any physician interested in the performance and interpretation of lymphograms.

Theodore E. Keats, M.D.

BOOKS RECEIVED

Radionuclide Studies of the Gastrointestinal System. Edited by Leonard M. Freeman, M.D., Associate Professor of Radiology, Albert Einstein College of Medicine, Bronx, N. Y.; and M. Donald Blaufox, M.D., Ph.D., Associate Professor of Medicine and Radiology, Albert Einstein College of Medicine, Bronx, N. Y. Cloth. Pp. 208, with many figures. Price, $13.75. Grune & Stratton, Inc., 111 Fifth Avenue, New York, N. Y. 10003, 1973.

The Interrelationship of the Immune Response and Cancer. Proceedings of the Seventh Annual San Francisco Cancer Symposium. Frontiers of Radiation Therapy and Oncology. Volume 7. Editor, Jerome M. Vaeth, San Francisco, Calif. Cloth. Pp. 222, with 48 figures. Price, $19.50. University Park Press, Chamber of Commerce Building, Baltimore, Md. 21202, 1972.

Tumors of the Central Nervous System. By Lucien J. Rubinstein, M.D., Professor of Pathology (Neuropathology), Stanford University School of Medicine, Stanford, Calif. Atlas of Tumor Pathology. Second Series, Fascicle 6. Published by the Armed Forces Institute of Pathology, Washington, D. C., under the auspices of Universities Associated for Research and Education in Pathology, Inc., Bethesda, Md. Paper. Pp. 400, with many figures. For sale by the American Registry of Pathology, Armed Forces Institute of Pathology, Washington, D. C. 20305, 1972.

Radiologic Examination of the Urinary Tract. By Howard M. Pollack, M.D., Associate Professor of Radiology, Temple University School of Medicine, and Director, Department of Radiology, Episcopal Hospital, Philadelphia, Pa. Reprinted from Karafin and Kendall's Urology, Volume I in Practice of Surgery. Cloth. Pp. 164, with 145 illustrations. Price, $8.50. Harper & Row, Publishers, Inc., 2350 Virginia Avenue, Hagerstown, Md. 21740, 1972.

The Essentials of Roentgen Interpretation. Third edition. By Lester W. Paul, M.D., Professor of Radiology, the University of Wisconsin Medical School; and John H. Juhl, M.D., Professor of Radiology and Chairman of the Department of Radiology, the University of Wisconsin Medical School. Cloth. Pp. 1,144, with 1,323 illustrations. Price, $35.00. Harper & Row, Publishers, Inc., 2350 Virginia Avenue, Hagerstown, Md. 21740, 1972.

Manual Lifting and Related Fields: an Annotated Bibliography. By John R. Brown, B.Sc., Ph.D. (Lond.), D.Sc. (Lond.), M.D. (Lond.), B.S., F.R.C.P.(C). Paper. Pp. 583, with some graphs. Labour Safety Council of Ontario, Ontario Ministry of Labour. Labour Safety Council of Ontario, 400 University Avenue, Toronto, Ontario, Canada, 1972.

SOCIETY PROCEEDINGS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Ted F. Leigh, Emory University Clinic, Atlanta, Ga. 30322. Annual Meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 25–28, 1973.

American Radium Society
Secretary, Dr. Felix N. Rutledge, M. D. Anderson Hospital and Tumor Institute, Houston, Texas 77025. Annual Meeting: Broadmoor Hotel, Colorado Springs, Colorado, April 22–26, 1973.

Radiological Society of North America
Secretary, Dr. Hillier L. Baker, Jr., Mayo Clinic, Rochester, Minn. 55901. Annual Meeting: Palmer House, Chicago, Ill., November 25–30, 1973.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago, Ill. 60606. Annual meeting: San Francisco, Calif., April 2–7, 1973.

Section on Radiology, American Medical Association
Secretary, Dr. Antolin Raventos, Davis, Calif. Annual Meeting: New York, N. Y., June 24–28, 1973.

American Board of Radiology
Secretary, Dr. C. Allen Good. Correspondence should be directed to Kahler East, Rochester, Minn. 55901.

Oral examinations will be held in the following cities during the next 2 years: Chicago, Ill., June 4–8, 1973, Marriott Motor Hotel; Dallas, Tex., Dec. 3–7, 1973, Statler Hilton Hotel; New York, N. Y., June 10–14, 1974, New York Hilton Hotel; and Los Angeles, Calif., Dec. 9–13, 1974, International Hotel.

Written examinations are scheduled in 13 large centers on June 16, 1973.

Applications must be received in the Board Office before Sept. 30 of the year preceding the one in which the candidate wishes to be examined.

Deadline for filing applications for any examination in 1974 is September 30, 1973.

American Board of Nuclear Medicine, Inc. A Conjoint Board of the American Boards of Internal Medicine, Pathology and Radiology and sponsored by the Society of Nuclear Medicine.
Chairman, Dr. Merrill A. Bender, Suite 2402, 211 E. 43rd St., New York, N. Y. 10017.

Examination for certification in the Specialty of Nuclear Medicine will be given April 7, 1973. The deadline for filing application forms was January 1, 1973.

American Association of Physicists in Medicine
Secretary, D. John Wright, Ph.D., Department of Radiology, Temple Univ. Health Sciences Center, Philadelphia, Pa. 19140. Annual Meeting in San Diego, Calif., July 29–Aug. 3, 1973.

American Society of Therapeutic Radiologists
Secretary, Dr. Herman D. Suit, Radiation Medicine, Massachusetts General Hospital, Boston, Mass. 02114. Annual Meeting.

American Institute of Ultrasound in Medicine
Secretary, John M. Reid, Ph.D., 556 18th Ave., Seattle, Wash. 98122. Annual Meeting.

American Society of Neuroradiology
Secretary, Dr. David O. Davis, Department of Radiology, 901 Twenty-third St., N. W., Washington, D. C. 20037. Annual Meeting, Boston, Mass., April 26–28, 1973.

Thirteenth International Congress of Radiology
President-Elect, Dr. Juan Gómez López. *Secretary General*, Dr. José Bonmatí, Lagasca, 27 Madrid 1, España. Meeting: Madrid, Spain, Oct. 15–20, 1973.

International Society of Radiology
Hon. Secretary-Treasurer, Prof. Eric Samuel, Radiologist-in-Charge, The Royal Infirmary, Edinburgh EH3 9Y-W, Scotland.

Eleventh Inter-American Congress of Radiology
Counselor for the United States, Dr. Juan A. del Regato, Penrose Cancer Hospital, 2215 North Cascade Ave., Colorado Springs, Colorado 80907. Meeting: Bogotá, Colombia in 1975.

Inter-American College of Radiology
President, Dr. Miguel Dao y Dao, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A.
Secretary General, Dr. Rubén Merenfeld, Instituto Diagnóstico, Apartado Postal 14213, Candelaria, Caracas, Venezuela, S.A. Meeting: Bogotá, Colombia in 1975.

Third Congress of the European Association of Radiology
Meeting in June, 1975 in Edinburgh, Scotland.

Second Asian and Oceanian Congress of Radiology
Honorary Secretary, Dr. J. J. Martin, Box 805 F., G.P.O., Melbourne, 3001, Australia.
Meeting in 1975.

Alabama Chapter of ACR
Secretary-Treasurer, Dr. Lowry R. Young, Jr., 905 Madison St., Huntsville, Ala. 35801. Meets time and place of Alabama State Medical Association.

Alaska Radiological Society
Secretary, Dr. Bruce C. Wright, Providence Hospital, Anchorage, Alaska. Meets third Wednesday each month.

American Thermographic Society
Secretary-Treasurer, Dr. Marc. S. Lapayowker, Department of Radiology, Temple Univ. Hosp., 3401 N. St., Philadelphia, Pa. 19140. Meets at New York-Hilton Hotel, June 23 and 24, 1973.

Arizona Radiological Society, Chapter of ACR
Secretary, Dr. Wesley S. Fee, 2421 E. 6th St., Tucson, Ariz. 85719. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Ark-La-Tex Radiological Society
Secretary, Dr. Erich K. Lang, Confederate Memorial Medical Center, LSU School of Medicine, Shreveport, La. 71101.

Arkansas Chapter of ACR
Secretary-Treasurer, Dr. David H. Newbern, 4301 W. Markham, Little Rock, Ark. 72205. Meets twice annually, the Spring Meeting being in conjunction with and at the place of the State Medical Association.

Association of University Radiologists
Secretary-Treasurer, Dr. Melvyn H. Schreiber, 2909 Dominique Dr., Galveston, Tex. Annual Meeting, Vancouver, B. C., Canada, May 9–12, 1973.

Atlanta Radiological Society
Secretary-Treasurer, Dr. Ernst Ruder, Dept. of Radiol., Crawford Long Memorial Hosp., Atlanta, Ga. 30308. Meets on four Thursday evenings during the academic year at a time announced in early September of each year, at the Academy of Medicine, Atlanta, Ga., at 8:00 P.M.

Bavarian-American Radiologic Society
Secretary, Lucien F. Burke, Maj. MC, Radiol. Service, US Army Gen. Hosp., Frankfurt, APO, New York 09757. Next Meeting: Torrejon, Spain (near Madrid, USAF Hospital, APO New York 09283), Apr. 11–16, 1973.

Blockley Radiological Society
Secretary-Treasurer, Dr. R. John Gould, 41 Lombardy Rd., Drexel Hill, Pa. 19026.

Bluegrass Radiological Society
Secretary-Treasurer, Dr. Eugene Slusher, Lexington

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Clinic, 1221 S. Broadway, Lexington, Ky. 40504. The Society meets once each month during the school year.

BRONX RADIOLOGICAL SOCIETY, NEW YORK STATE, CHAPTER ACR
Secretary-Treasurer, Dr. Leon J. Corbin, 1369 Rosedale Ave., Bronx, N. Y. 10472. Meets 4 times a year.

BROOKLYN RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Sarah Lieberson, 1298 St. Marks Ave., Brooklyn, N. Y. 11213. Meets first Thursday of each month, October through June.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Ru-Kan Lin, 191 North St., Buffalo, N. Y. 14201. Meets second Monday evening each month, October to May inclusive, at University Club.

CALIFORNIA RADIATION THERAPY ASSOCIATION
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets semiannually in San Francisco and Los Angeles.

CALIFORNIA RADIOLOGICAL SOCIETY, CALIFORNIA CHAPTER OF ACR
Secretary-Treasurer, Dr. John L. Gwinn, 4650 Sunset Blvd., Los Angeles, Calif. 90027.

CATAWBA VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. Emmett R. White, P.O. Box 10, Rutherford College, N. C. 28671. Meets every Thursday, Dept. of Radiology, Valdese General Hosp., Valdese, N. C., at 12:30 P.M.

CENTRAL NEW YORK RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. John Sanborn, Radiology Department, Crouse-Irving Memorial Hosp., Irving Ave., Syracuse, N. Y. 13210. Meets first Monday each month October through May.

CENTRAL OHIO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Terry Meyer, 175 S. Merkle Rd., Columbus, Ohio 43209. Meets second Thursday in October, November, January, and March 15, and May 19 at Fort Hayes Hotel, Columbus, Ohio.

CHICAGO RADIOLOGICAL SOCIETY, DIVISION OF THE ILLINOIS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Raymond L. Del Fava, 355 Ridge Ave., Evanston, Ill. 60202. Meets third Thursday of each month, October to April, except December, at the Bismarck Hotel, Chicago, Ill.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Alvin Segel, 3395 Scranton Rd., Cleveland, Ohio 44109. Meetings at 7:00 P.M. on fourth Monday of October, November, January, February, March and April.

COLORADO RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Jerome D. Sutherland, 3705 E. Colfax Ave., Denver, Colo. 80206. Meets third Friday of each month at Denver Athletic Club from September through May.

CONNECTICUT VALLEY RADIOLOGIC SOCIETY
Secretary, Dr. Gerald N. LaPierre, 759 Chestnut St., Springfield, Mass. 01107. Meets in April and October.

DALLAS-FORT WORTH RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Lee Radford, 6011 Harry Hines, Suite 900, Dallas, Tex. 75235. Meets the 3rd Monday of every month at 6:30 P.M., at the Cibola Inn, Arlington, Tex.

DELAWARE CHAPTER OF ACR
Secretary, Dr. Seymour R. Kaplan, Kent Gen. Hosp., Dover, Del. 19901.

EAST BAY RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Peter E. Kane, Children's Hosp. Med. Ctr., Oakland, Calif. 94609. Meets first Thursday each month, Oct. through May, at University Club, Oakland, Calif.

EAST TENNESSEE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. George H. Wood, 205 Medical Arts Bldg., Knoxville, Tenn. 37902. Meets in January and September.

FLORIDA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Ralph C. Aye, Tampa General Hospital, Tampa, Fla. 33606. Meets twice annually, in the spring with the annual State Society Meeting and in the fall.

FLORIDA WEST COAST RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. J. C. Hewitt, 1 Davis Blvd., Tampa, Fla. 33606. Meets in January, March, May, July, September and November.

GEORGIA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary, Dr. Richard S. Colvin, Emory University Clinic, Atlanta, Ga. 30322. Meets in spring and fall at Annual State Society Meeting.

GREATER CINCINNATI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Owen L. Brown, 2421 Auburn Ave., Cincinnati, Ohio 45219.

GREATER LOUISVILLE RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. L. D. LeNeave, 315 E. Broadway, Louisville, Ky. 40202. Meets monthly.

GREATER MIAMI RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Stanley I. Worton, 1400 N.W. 10th Avenue, Miami, Florida 33136. Meets monthly, third Wednesday at 8:00 P.M. at various member hospitals, Miami, Fla.

GREATER ST. LOUIS SOCIETY OF RADIOLOGISTS
Secretary-Treasurer, John J. Lang, 507 Fairways Circle, St. Louis, Mo. 63141.

HAWAII RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Raymond W. Brust, Jr., St. Francis Hosp., 2260 Liliha St., Honolulu, Hawaii 96817. Meets third Monday of each month at 7:30 P.M.

HEALTH PHYSICS SOCIETY
Secretary, Shirley D. Vickers, Catholic Medical Center of Brooklyn and Queens, 88-25 153rd St., Jamaica, N. Y. 11432. Annual Meeting: Deauville Hotel, Miami Beach, Fla., June 17–21, 1973.

HOUSTON RADIOLOGICAL SOCIETY
Secretary, Dr. Neill B. Longley, 6436 Fannin, Suite 601, Houston, Tex. 77025. Meets fourth Monday of each month, except June, July, August and December, at 6:00 P.M., at 103 Jesse H. Jones Library Building, Texas Medical Center, Houston, Tex. 77025.

IDAHO STATE RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Hugh P. Smith, Jr., 130 E. Bannock, Boise, Id. 83702. Meets in the spring and fall.

ILLINOIS RADIOLOGICAL SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. B. Jay Hill, Mercy Hospital, Stevenson at King Drive, Chicago, Ill. 60616. Meets in the spring and fall.

INDIANA ROENTGEN SOCIETY, INC., CHAPTER OF ACR
Secretary, Dr. L. Ray Stewart, 852 S. Alvord Blvd., Evansville, Ind. 47714.

IOWA RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. John Huston Jr., 1948 First Ave. N.E., Cedar Rapids, Iowa 52402. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

KANSAS RADIOLOGICAL SOCIETY, CHAPTER OF ACR
Secretary-Treasurer, Dr. Ralph H. Baehr, 310 Medical Arts Bldg., Topeka, Kan. 66604. Meets in spring with State Medical Society and in winter on call.

KENTUCKY CHAPTER OF ACR
Secretary-Treasurer, Dr. Joseph G. Whelan, Jr., 1313 St. Antony Place, Louisville, Ky. 40204. Meets in April and September.

KINGS COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. Sidney Hendler, 1880 Ocean Ave., Brooklyn 30, N.Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

KNOXVILLE RADIOLOGICAL SOCIETY
Secretary, Dr. Clifford L. Walton, Blount Professional Bldg., Knoxville 20, Tenn. Meetings are held the third Monday of every other month at the University of Tennessee Memorial Research Center and Hospital.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Jerome Zwanger, 1200 Stewart Ave., Garden City, N. Y. 11533. Meets monthly.

Los Angeles Radiological Society
Secretary, Dr. Gabriel H. Wilson, UCLA Center for Medical Sciences, Los Angeles, Calif. 90024. Meets second Wednesday of month in September, November, January, April and June at Los Angeles County Medical Association Building, Los Angeles, Calif. Midwinter Radiological Conference.

Louisiana Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Robert T. Cook, Southern Baptist Hosp., 2700 Napoleon Ave., New Orleans, La. 70115.

Louisiana-Texas Gulf Coast Radiological Society
Secretary-Treasurer, Dr. Edward A. Sheldon, 109 Doctors Bldg., Beaumont, Tex. 77701.

Maine Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Richard W. Taylor, Radiology Department, St. Mary's General Hospital, Lewiston, Maine 04240. Meets in June, September, December and April.

Maryland Radiological Society, Chapter of ACR
Secretary, Dr. George Burke, 4000 North Charles St., Baltimore, Md. 21218.

Massachusetts Radiological Society, Chapter of ACR
Secretary, Dr. Norman L. Sadowsky, The Faulkner Hosp., 1153 Centre St., Jamaica Plain, Mass. 02130.

Memphis Roentgen Society
Secretary-Treasurer, Dr. Jerry C. Phillips, The University of Tennessee College of Medicine, Department of Radiology, Walter C. Chandler Bldg., 865 Jefferson Ave., Memphis, Tenn. 38103. Meets first Monday Oct. through May at the University Club.

Miami Valley Radiological Society
Secretary, Dr. Bert Must, I.B.M. Bldg., Dayton, Ohio. Meets third Thursday of fall, winter and spring months at 7:30 P.M. at Miami Valley Hospital, Dayton, Ohio.

Michigan Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. George A. Kling, Harper Hospital, 3825 Brush St., Detroit, Mich. 48201. Meets monthly, first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

Mid-Hudson Radiological Society
Secretary-Treasurer, Dr. Herbert S. Berlin, Hopewell Junction, N. Y. Meets 7:00 P.M., first Wednesday of each month, September to May.

Milwaukee Roentgen Ray Society
Secretary-Treasurer, Dr. Thomas C. Lipscomb, 1004 North Tenth St., Milwaukee, Wis. 53233. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Harlan W. Hawkinson, 6 Buffalo Rd., St. Paul, Minn. 55110. Meets twice annually, fall and winter.

Mississippi State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Nancy W. Burrow, 1327 Peachtree St., Jackson, Miss. 39202. Meets third Thursday of each month at the Heidelberg Hotel, Jackson, at 6:00 P.M.

Missouri Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ronald G. Evens, Mallinckrodt Institute of Radiology, 510 S. Kingshighway, St. Louis, Mo. 63110.

Montana Radiological Society, Chapter of ACR
Secretary, Dr. Dexter W. Johnson, Columbus Hosp., Great Falls, Mont. 59401.

Nebraska Chapter of ACR
Secretary-Treasurer, Dr. J. F. Johnson, 1808 North 100th St., Omaha, Neb. 68114. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

Nevada Radiological Society, Chapter of ACR
Secretary, Dr. William G. Arbonies, 887 Marsh, Reno, Nev. 89520.

New England Roentgen Ray Society
Secretary, Dr. Stefan C. Schatzki, 1180 Beacon St. Brookline Mass. 02146. Meets the third Friday of each month, October through April, excluding December, at The Longwood Towers, 20 Chapel Street, Brookline, Mass., at 4:30 P.M.

New Hampshire Roentgen Ray Society, Chapter of ACR
Secretary-Treasurer, Dr. Edward P. Kane, Claremont Gen. Hosp., Claremont, N. H. 03743. Meets four to six times yearly.

New Mexico Society of Radiologists, Chapter of ACR
Secretary, Dr. Carole R. Simmons, Dept. of Radiol., Presbyterian Hospital Center, Albuquerque, N. M. 87106. Four meetings annually, three held in Albuquerque, N. M., and one held at time and place of New Mexico State Medical Society annual meeting.

New Orleans Radiological Society, Inc.
Secretary-Treasurer, Dr. Jimmy L. Mains, P.O. Box 446, Gretna, La. 70053. Meets bimonthly at local restaurants selected by the President.

New York Roentgen Society
Secretary-Treasurer, Dr. Howard R. Gould, 153 West 11th Street, New York, N. Y. 10011. Meets monthly on the 3rd Monday at the New York Academy of Medicine at 4:30 P.M. Annual Spring Conference, Waldorf-Astoria Hotel, New York, N. Y., Apr. 26–28, 1973. Further information may be obtained from Dr. Albert A. Dunn, Roosevelt Hosp., New York, N. Y. 10019.

New York State Chapter of ACR
Secretary Treasurer, Dr. John J. Magovern, 74 N. Village Ave., Rockville Centre, N. Y. 11570.

North Carolina Chapter of ACR
Secretary-Treasurer, Dr. Ernest B. Spangler, Wesley Long Hosp., Greensboro, N. C. 27402. Meets twice a year. The Spring Meeting is held at the time of the meeting of the North Carolina Medical Society. The Fall Meeting is held in November at the Mid Pines Club, Southern Pines, N. C.

North Dakota Radiological Society, Chapter of ACR
Secretary, Dr. Marshall Landa, 1702 13th St., So., Fargo, N. D. 58102. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. David F. Bew, University Hospital of Jacksonville, 655 W. Eighth Street, P.O. Box 2751, Jacksonville, Florida 32203. Meets quarterly in March, June, September and December.

Northeastern Oklahoma Radiological Society
Secretary-Treasurer, Dr. Theodore J. Brickner, Jr., 5919 S. Gary Place, Tulsa, Okla. 74110.

Northeastern New York Radiological Society
Secretary, Dr. Robert C. Friedman, 325 Presidential Way, Guilderland, N. Y. 12085. Meets in Albany area on third Wednesday of October, November, March, April, and May.

Northern California Radiation Therapy Association
Secretary-Treasurer, Dr. James R. Eltringham, Stanford Medical Center, Stanford, Calif. 94304. Meets quarterly.

Northern California Radiological Society
Secretary, Dr. J. Richard McProuty, 6620 Coyle Ave., Carmichael, Calif. 95608. Meets fourth Monday of Nov., Jan., and March at the Mansion Inn, Sacramento, Calif.

Northwestern New York Radiological Society
Secretary, Dr. Barbara E. Chick, Glens Falls Hospital, Glens Falls, N. Y. 12801.

Northwestern Ohio Radiological Society
Secretary, Dr. Vito J. Zupa, Mercy Hospital, Department of Radiology, Toledo, Ohio.

Ohio State Radiological Society, Chapter of ACR
Secretary, Dr. Thomas F. Ulrich, Barberton Citizens Hospital, Barberton, Ohio 44203.

Oklahoma State Radiological Society, Chapter of ACR
Secretary, Dr. George H. Ladd, 4616 Denison, Muskogee, Okla. 74401. Meets in January, May and October.

Orange County Radiological Society
Secretary, Dr. Norman Arnett, 400 North Pomona, Fullerton, Calif. 92632. Meets on fourth Tuesday of the month, excluding June, July, August, and December, at the Orange County Medical Association Bldg., Orange, Calif.

Oregon State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Ronald W. Philips, 2305 Washington, Milwaukie, Ore. 97222. Meets on second Wednesday of month, October through April, at the University Club, Portland, Ore.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans, La. 70113. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary-Treasurer, Dr. Robert S. Miller, 13753 S.W. Farmington Rd., Beaverton, Oregon 97005. Annual meeting: Benson Hotel, Portland, Ore., May 11–13, 1973.

Pennsylvania Radiological Society, Chapter of ACR
Secretary, Dr. Theodore A. Tristan, Harrisburg Polyclinic Hosp., Harrisburg, Pa. 17105.

Philadelphia Roentgen Ray Society
Secretary, Dr. Howard M. Pollack, Department of Radiology, Episcopal Hospital, Philadelphia, Pa. 19125. Meets first Thursday of each month at 5 P.M., from October to May in Thompson Hall, College of Physicians.

Pittsburgh Roentgen Society
Secretary, Dr. Stephen C. Bruno, Shadyside Hospital, 5230 Centre Ave., Pittsburgh, Pa. 15232. Meets second Wednesday of month, September through May, at the Pittsburgh Athletic Association.

Radiation Research Society
Executive Secretary, Richard J. Burk, Jr., 4211 39th St., N.W., Washington, D. C. 20016. Annual Meeting: St. Louis, Mo., April 29–May 3, 1973. International Congress of Radiation Research, Seattle, Wash., July 14–20, 1974.

Radiological Society of Connecticut, Inc., Chapter of ACR
Secretary-Treasurer, Dr. Carl W. Scheer, 335 Cook Ave., Meriden, Conn. 06450. Meetings are held quarterly.

Radiological Society of Greater Cincinnati
Secretary-Treasurer, Dr. Alvin Nathan, c/o Academy of Medicine, 320 Broadway, Cincinnati, Ohio 45202. Meets first Monday of each month at Cincinnati Academy of Medicine.

Radiological Society of Greater Kansas City
President-Secretary, Dr. Arch W. Templeton, Univ. of Kansas Med. Ctr., Kansas City, Kansas 66103. Meets 5 times a year on given dates.

Radiological Society of Louisiana, Chapter of ACR
Secretary-Treasurer, Dr. Robert T. Cook, 1820 Octavia St., New Orleans, La. 70115. Meets semiannually during Louisiana State Medical Society meeting and 6 months later.

Radiological Society of New Jersey, Chapter of ACR
Secretary, Dr. Sidney Ketyer, St. Elizabeth Hosp., 225 Williamson St., Elizabeth, N. J. 07207. Meets in Atlantic City at time of State Medical Society meeting and in October or November in Newark, N. J.

Radiological Society of Rhode Island, Chapter of ACR
Secretary-Treasurer, Dr. Daniel J. Hanson, 116 Nayatt Rd., West Barrington, R. I. 02806.

Radiological Society of Southern California
Secretary-Treasurer, Dr. Marshall Rowen, Dept. Radiol., St. Joseph Hosp., 1100 Stewart Dr., Orange, Calif. 92668. Meets three times a year, usually October, February and May.

Radiological Society of the State of New York
Secretary-Treasurer, Dr. John W. Colgan, 273 Hollywood Ave., Rochester, N. Y. 14618.

Redwood Empire Radiological Society
Secretary, Dr. Lee F. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

Richmond County Radiological Society
Secretary, Dr. Donald P. King, 218 Gun Club Rd., Richmond, Va. 23221. Meets first Thursday of each month at various hospitals.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary-Treasurer, Dr. Kenneth E. Robinson, 1441 East Avenue, Rochester, New York 14610. Quarterly meetings on the call of the President, at the Rochester Academy of Medicine.

Rocky Mountain Radiological Society
Secretary-Treasurer, Dr. Lorenz R. Wurtzebach, 4200 E. Ninth Ave., Denver, Colo. 80220. Annual meeting: Brown Palace Hotel, Denver, Colo., Aug. 2–4, 1973.

San Antonio-Civilian Military Radiological Society
Secretary, Dr. Robert M. Maurer, Santa Rosa Medical Center, San Antonio, Tex. 78207. Meets third Wednesday of each month at Fort Sam Houston Officers' Club at 6:30 P.M.

San Diego Radiological Society
President, James R. Collins, 340 Fourth Ave. Suite 15, Chula Vista, Calif. 92010. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary-Treasurer, Dr. James G. Moore, Mary's Help Hospital, 1900 Sullivan Ave., Daly City, Calif. 94015.

Section on Radiology, California Medical Association
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

Section on Radiology, Medical Society of the District of Columbia
Secretary-Treasurer, Dr. Louis Wener, Cafritz Memorial Hosp., 1310 Southern Ave., S.E., Washington, D. C. 20032. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

Section of Radiology, National Medical Association
Chairman, Dr. Henry W. Wiggins, Jr., Mercy Hosp., 2537 South Prairie Ave., Chicago, Ill. 60616. Annual Meeting: New York, N. Y., Aug. 11–16, 1973.

Section on Radiology, Southern Medical Association
Secretary, Dr. Mario A. Calonje, 1514 Jefferson Highway, New Orleans, La. 70121. Annual Meeting.

Section on Radiology, Texas Medical Association
Secretary, Dr. George F. Crawford, St. Elizabeth Hospital, Beaumont, Tex. Meets annually with the Texas Medical Association.

Shreveport Radiological Club
Secretary, Dr. W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday at 7:30 P.M., September to May inclusive.

Society for Pediatric Radiology
Secretary, Dr. John L. Gwinn, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027. Annual meeting: Queen Elizabeth Hotel, Montreal, P. Q., Canada, September 23–24, 1973.

Society of Gastrointestinal Radiologists
Secretary-Treasurer, Dr. Wm. B. Seaman, The Presbyterian Hospital, Columbia-Presbyterian Medical Center, 622 W. 168th St., New York, N. Y. 10032.

Society of Nuclear Medicine
Secretary, Dr. E. James Potchen, Edward Mallinckrodt Institute of Radiology, 660 S. Euclid Ave., St. Louis, Mo. 63110. *Administrative Officer*, Mrs. Margaret Glos, 211 E. 43rd St., New York, N. Y. 10017. Annual meeting: Americana Hotel, Miami Beach, Fla., June 12–15, 1973.

South Bay Radiological Society
Secretary, Dr. Virgil H. Voss, 900 Kiely Blvd., Santa Clara, Calif. 95051. Meets the 2nd Monday of each month at the Santa Clara County Medical Association Bldg., 700 Empey Way, San Jose, Calif.

South Carolina Radiological Society, Chapter of ACR
Secretary, Dr. George W. Brunson, 1406 Gregg St., Columbia, S. C. Annual meeting (primarily business) in conjunction with the South Carolina Medical Associa-

tion meeting in May. Annual fall scientific meeting at time and place designated by the president.

South Coast Radiological Society
Secretary-Treasurer, Dr. James T. McClintock, P.O. Box 837, Santa Barbara, Calif. 93102. Meets fourth Monday of the month, Oct. through May.

South Dakota Radiological Society, Chapter of ACR
Secretary, Dr. M. F. Petereit, 2416 S. Phillips, Sioux Falls, S. D. 57105. Meets in spring with State Medical Society and in fall.

Southern California Radiation Therapy Society
Secretary-Treasurer, Dr. John Byfield, 1000 West Carson St., Torrance, Calif. 90502. Meets quarterly.

Southern Radiological Conference
Secretary-Treasurer, Dr. Marshall Eskridge, Mobile Infirmary, P.O. Box 7544, Mobile, Ala. 36607.

Southwestern Radiological Society
Secretary, John M. McGuire, 904 Chelsea, El Paso, Tex. Meets last Monday of each month at 6:30 P.M. in the Paso del Norte Hotel.

Tennessee Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Carl T. Stubblefield, Bedford County Hospital, Columbia, Tenn. 38401. Meets annually at the time and place of the Tennessee State Medical Association meeting.

Texas State Radiological Society, Chapter of ACR
Secretary, Dr. Herman C. Sehested, 815 Medical Tower, Room 100, 1550 W. Rosedale St., Fort Worth, Tex. 76104. Annual meeting.

The Fleischner Society
President, Dr. Robert G. Fraser, 1555 Summerhill Ave., Montreal 109, P.Q., Canada. Annual meeting.

Tri-State Radiological Society
Secretary, Dr. John H. Marchand, Jr., Methodist Hospital, Henderson, Ky. Meets third Wednesday of Oct., Jan., March and May, 8:00 P.M., Elks Club in Evansville, Ind.

Upper Peninsula Radiological Society
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

Utah State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John F. Stucki, Department of Radiology, McKay-Dee Hosp., 3939 Harrison Blvd., Ogden, Utah 84403. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Vermont Radiological Society, Chapter of ACR
Secretary, Dr. J. Lorimer Holm, R.R.#3, Barre, Vt. 05641.

Virginia Chapter of ACR
Secretary-Treasurer, Dr. James S. Redmond, Suite 7, Medical Center, Lynchburg, Va. 24501. Next Meeting: Nov. 6, 1972 at the Conference Ctr., Williamsburg, Va.

Washington, D. C., Chapter of ACR
Secretary-Treasurer, Dr. Albert M. Zelna, 9110 Seven Locks Rd., Bethesda, Md. 20014.

Washington State Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. John N. Roehr, 1011 Medical Dental Bldg., Seattle, Wash. 98101.

West Virginia Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Andrew W. Goodwin, II, 200 Med. Arts Bldg., Charleston, W. Va. 25301. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester County Radiological Society
Secretary, Dr. Max C. King, 314 Woodland Hills Rd., White Plains, N. Y. 10603. Meets on second Tuesday of October, December, February and May.

Wisconsin Radiological Society, Chapter of ACR
Secretary-Treasurer, Dr. Marvin L. Hinke, 630 S. Central Ave., Marshfield, Wisc. 54449. Meets twice a year, May and September.

Wisconsin Society of Therapeutic Radiologists
Secretary, Dr. Robert W. Edland, Gundersen Clinic, LaCrosse, Wisc. 54601. Meets quarterly.

Wyoming Radiological Society, Chapter of ACR
Secretary, Dr. Ross J. Collie, Box 96, Lander, Wyo. 82520. Meets in fall with State Medical Society and in spring on call of President.

Mexico, Puerto Rico and Central America

Asociación Costarricense de Radiología
Secretary, Dr. Francisco Mirambell S. Apartado 3352, San José, Costa Rica.

Asociación de Radiólogos de Centro America y Panamá. Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá
Secretary-General, Dr. Francisco Mirambell, Apartado 3352, San José, Costa Rica, Central America.
Meets annually in a rotating manner in the six countries.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad de Radiología de El Salvador
Secretary, Dr. Carlos Mejia, 5a Av. Nte. No. 434, San Salvador, Rep. El Salvador.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad Mexicana de Radiología, A.C.
Coahuila No. 35, México 7, D.F., México.
Secretary-General, Dr. Jorge Cano Coquí. Meets first Monday of each month.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital chosen at preceding meeting.

Sociedad Radiológica de Puerto Rico
Secretary, Dr. Heriberto Pagán Sáez, Box 9387, Santurce, Puerto Rico. Meets second Thursday of each month at 8:00 P.M. at the Puerto Rico Medical Association Bldg. in San Juan.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Moyne, 121 Boul. Taschereau, Greenfield Park, P.Q., Canada. Meets four times a year.

British Institute of Radiology
Honorary Secretary, Dr. T. Kerr, 32 Welbeck St., London, W1M/7PG, England. Meets monthly from October until May.

Canadian Association of Physicists, Division of Medical and Biological Physics
Honorary Secretary-Treasurer, Dr. R. G. Baker, Ontario Cancer Foundation, Ottawa Civic Clinic, 1053 Carling Ave., Ottawa 3, Ont., Canada.

Canadian Association of Radiologists
Honorary Secretary, Dr. Champlain Charest, 1555 Summerhill Ave., Montreal 109, Que., Canada. Annual meeting: Montreal, Que., Canada, March 11–17, 1973.

Edmonton and District Radiological Society
Secretary, Dr. L. A. Koller, Suite 360, Professional Bldg., 10830 Jasper Ave., Edmonton 15, Alberta, Canada. Meets third Thursday of each month October to May, except December, at various Edmonton Hospitals.

Faculty of Radiologists
Honorary Secretary, Robert Morrison, 47 Lincoln's Inn Fields, London, W.C.2, England. The scientific meetings held in January, February and March 1973 will be combined sessions with the British Institute of Radiology and the Section of Radiology of The Royal Society of Medicine.

Faculty of Radiologists, Royal College of Surgeons in Ireland
Hon. Secretary, Dr. D. F. Canwell, 123 St. Stephens Green, Dublin 2, Ireland.

Montreal Radiological Study Club
Secretary, Dr. W. Paul Butt, Montreal General Hospital, Montreal, Que., Canada. Meets first Tuesday evening, October to April.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 8:15 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1 M&AE, 1 England.

Société Canadienne-Française de Radiologie
Secretary General, Dr. Hubert Sasseville, Verdun Hospital, Montréal, P.Q., Canada. Meets every third Tuesday from October to April.

The Hospital Physicists' Association
Honorary Secretary, J. B. Massey, B.Sc., Christie Hosp. and Holt Radium Institute, Physics Department, Withington, Manchester M20 9BX, England.

Toronto Radiological Society
Secretary, Dr. George Wortzman, Toronto General Hosp., Toronto 12, Ont., Canada. Meets second Monday of each month, September through May.

Royal College of Radiologists of Australasia
Honorary Secretary, Dr. T. P. Loneragan, 147 Macquarie St., Sydney, N.S.W. 2000, Australia.

South America

Colégio Brasileiro de Radiologia
Secretary-General, Dr. Miguel Mario Céntola, Caixa Postal 5984, São Paulo, Brazil.

Federación Argentina de Sociedades de Radiología
Branches of the Federation are: Sociedad de Radiólogos de la Provincia de Córdoba; Sociedad Argentina de Radiología; Asociación Argentina de Radiología; Sociedad de Radiología, Radioterapéutica y Medicina Nuclear de Rosario; Sociedad de Radiología y Medicina Nuclear del Centro y Sudeste de la Provincia de Buenos Aires (Mar del Plata); Sociedad Salteña de Radiología y Medicina Nuclear; Sociedad de Radiología de Tucumán; Sociedad de Radiologia del Nordeste Argentino; Sociedad de Radiología de La Plata; and Sociedad de Radiología de San Juan.
Secretary-General-Treasurer, Dr. Roberto Habichayn, Av. Colón 637, Córdoba, Argentina.

Sociedad Argentina de Radiología
Secretary-General, Dr. Tomás J. Gutiérre E, Santa Fé 1171 Buenos Aires, Argentina. Meets first Wednesday evening, April through December.

Sociedad Boliviana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1182, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Armando Rocha Amoédo, Caixa Postal 1532, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Claudio Cortés, Casilla, 13426 Santiago, Chile. Meets first Friday of each month at Av. Santa María 1810 at 7:00 P.M.

Sociedad Colombiana de Radiologia
Secretary-General, Dr. Rodrigo Caro Molina, Cali, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología
Secretary, Dr. Carlos Palau Jimenez, Casilla 5469, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Hugo Volpe Rios, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary-General, Dr. Miguel Chiappori Cambana, Av. General Santa Cruz No. 315, Miraflores, Lima, Perú, Casilla Correo, 2306, Lima, Perú. Meets monthly except during January, February, and March.

Sociedad de Radiología del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiología.

Sociedad de Radiología del Nordeste Argentino
Secretary-General, Dr. Francisco J. Velar, Catamarca 561, Corrientes, Argentina.

Sociedad de Radiología de La Plata
Secretary, Dr. Hiram D. Haurigot, Calle 50 No. 374, La Plata, Argentina.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Manuel Gonzáles Maseda, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiología de Pernambuco
Secretary, Dr. Manoel Medeiros Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad de Roentgenología y Medicina Nuclear de la Provincia de Córdoba
Secretary-General, Dr. Lucas C. Di Rienzo, Ave. Grl. Paz. 151, Córdoba, Argentina.

Sociedad de Radiología, Radioterapéutica y Medicina Nuclear, de Rosario
Secretary-General, Dr. Federico Frágola, Santa Fe 1798, Rosario, Argentina.

Sociedad Salteña de Radiología y Medicina Nuclear
Secretary, Dr. Julio Luis Baldi, Av. Sarmiento 536, Salta, Argentina.

Sociedad Venezolana de Radiología y Medicina Nuclear
Secretary-General, Dr. Salvador Itriago Borgas, Apartado Postal 9213, Candelaria, Caracas, Venezuela. Meets monthly, third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
Secretary, Dr. Ernst Kotcher, Wiener Allgemeine Poliklinik Mariannengasse 10, A-1090 Wien, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik. The 1973 Annual Meeting is a joint meeting with the Deutsche Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Société Royale Belge de Radiologie
General Secretary, Dr. Joseph Baeyens, Alost, Belgium. Meets in February, March, May, June, September, October, November and December.

Société Européenne de Radiologie Pédiatrique
Secretary, Dr. P. Hicken, The Children's Hosp., Ladywood Middleway, Birmingham B16 8ET, Great Britain. Tenth Annual Meeting, Birmingham, April 11–13, 1973.
Permanent Secretary, Clément Fauré, Hôpital des Enfants-Malades, 149, rue de Sèvres, 75 Paris 15e, France.

Société Française de Radiologie Médicale, Médecine Nucléaire et Electrologie, and its branches: Société du Sud-Ouest, du Littoral méditerranéen, du Centre et Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et du Massif Central. Parent Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris, France.
Secretary-General, Dr. Ch. Proux, 9 rue Daru Paris 8e, France.

Société Française de Neuroradiologie
Secretary-General, Professeur agr. R. Djindjian 16, rue de l'Université 75, Paris 7e, France. Annual meeting.

Československá Radiologická Společnost
Secretary, Associate Professor Jaromír Kolář, M.D., Sc.D., Radiological Clinic, Praha 2, U nemocnice 2, Czechoslovakia. Meets monthly except during July, August and September. Annual general meeting.

Deutsche Röntgengesellschaft
President, Professor Dr. med. Walter Frommhold, Director of Medizinisches Strahleninstitut der Universität Tübingen, Röntgenweg 11, 7400 Tübingen, Germany. The 1973 Annual Meeting is a joint meeting with the Österreichische Röntgengesellschaft and will be held in Vienna, April 12–14, 1973.

Società Italiana di Radiologia Medica e Medicina Nucleare
Administrative Secretary, Prof. E. Conte, Ospedale Mauriziano, 10128 Torino, Italy. Meets annually.

Societas Radiologica Danica
Secretary, Dr. Bent Langefeldt, Tretommervej 20a, DK-8240 Risskov, Denmark.

Nederlandse Vereniging voor Radiologie
Secretary, Dr. J. D. Mulder, Dept. of Rad., Akademisch Ziekenhuis, Leiden, Netherlands.

Scandinavian Radiological Society
Secretary-General, Professor C. E. Unnérus, M.D., Hagalung-Tapiola, Havsvindsvägen 5 C., Finland.

Sociedad Española de Radiología y Electrología Médicas y de Medicina Nuclear
Secretary, Dr. José Bonmatí, Villanueva, 11, Madrid 1, España. Meets every second Friday of each month, Oct. to June, inclusive, in Madrid.

Sociedade Portuguesa de Radiologia e Medicina Nuclear
Secretary-General, Dr. Luís Aires de Sousa, Av. Elias Garcia, 123- 1, Esg.-Lisboa 1-Portugal.

Schweizerische Vereiningung für Radiologie, Nuklearmedizin und Strahlenbiologie (Association Suisse de Radiologie, Médecine Nucléaire et de Radiobiologie)
Secretary, Dr. med. Gustav Schoch, Bethesdaspital, Gellerstrasse 144, 4000 Basel, Switzerland.

Asia

Indian Radiological Association
Secretary, Dr. L. R. Parthasarathy, 44 Constable Road, Madras—23, India.

Indonesian Radiological Society
Secretary, Dr. Gani Iljas Sasmitaatmadja, Radiology Dep., Faculty of Medicine, University of Indonesia, Salemba 6, Djakarta, Indonesia.

Iranian Radiological Society
Secretary, Dr. Issa Yaghmai, P.O. Box No. 14-1151, Teheran, Iran. The Society meets on the second Saturday of each month. Third National Iranian Congress of Radiology: Isfahan, Iran, May 5–10, 1973. Deadline for acceptance of papers Feb. 20, 1973.

Israel Radiological Society
President, Dr. I. Izkovitch, 2 Wingate Ave., Beit Harofe, Haifa, Israel.

Japanese American Radiological Society
Secretary, Thomas J. Imray, Maj. MC, Chief, Radiol. Dep., US Army Hosp., Camp Zana, Japan, APO San Francisco, Calif. 96343. Meets 3rd Thursday, monthly at various locations in Tokyo.

Philippine College of Radiology
Secretary-Treasurer, Dr. Edmundo V. Villacorta, Box 1284, Commercial Center, Makati, Rizal D-708, Philippines. Meets every 3 weeks on Fridays. Annual convention.

Radiological Society of Thailand
Secretary, Prof. Rojana Suvansuthi, M.D., Ph.D., Depart. of Rad., Sirizaj Hospital, Faculty of Medicine, Mahidol University, Bangkok 7, Thailand.

Africa

Association of Radiologists of West Africa
Honorary Secretary, Dr. T. M. Kolawole, University College Hospital, University of Ibadan, Ibadan, Nigeria.

Radiological Society of South Africa
Secretary, Dr. B. Rosenberg, P.O. Box 3200, Johannesburg, South Africa.

South African International Radiological Congress
Director, Dr. Paul Sneider, P.O. Box 4878, Johannesburg, South Africa.

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ABSTRACTS OF RADIOLOGIC LITERATURE

E. FREDERICK LANG, M.D., Editor

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ROENTGEN DIAGNOSIS

Head

Finby, Nathaniel, and Kraft, Ernest. The aging skull: comparative roentgen study; 25 to 34 year interval. *Clin. Radiol.*, Oct., 1972, *23*, 410–414. (From: Department of Radiology, St. Luke's Hospital Center and Rockefeller University, New York, and the Veterans Administration Hospital, Northport, N. Y.)

The size of an adult skull has been considered stationary after completion of the adolescent growth period; yet, a man's head may require a larger hat size with advancing age. Such occurrence has formerly been ascribed to increased fatty tissue in the scalp. This article and recent reports, however, indicate that physiologic changes of the skull actually take place throughout life.

The authors have compared the skull roentgenograms in 72 adults at intervals ranging from 25 to 34 years. It was found that the paranasal sinuses became larger in 100 per cent and the cranial vault in 71 per cent of the cases; the cranial tables became thicker in 64 per cent and an enlargement of the sella turcica was detected in 45 per cent. Occasionally, an osteoporosis of the dorsum sellae was observed in the follow-up study. The findings confirmed a continuous activity of growth hormone in the aging skull.—*John H. Harris, M.D.*

Jerman, Albert C., Kinsley, Earl L., and Morris, Charles R. Absorbed radiation from panoramic plus bitewing exposures *vs.* full-mouth periapical plus bitewing exposures. *J. Am. Dent. A.*, Feb., 1973, *86*, 420–423. (Address: Albert C. Jerman, D.D.S., Dental Sciences Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235.)

In 1959 the panoramic dental radiographic machine was developed and it has permitted increase in speed, simplicity, and scope of dental examination with low radiation dosage. Since dental caries, however, is not sharply demarcated in panoramic roentgenograms, many dentists use bitewings in addition for a satisfactory demonstration, particularly of the posterior teeth.

The standard intraoral survey, made without the panoramic machine, consists of 14 films with the addition of 2 bitewings.

Four women and 4 men were subjected to each type of complete examination. Thermoluminescent dosimeters were implanted in resin mouth guards for each patient.

Sixteen dosimeters were used in each patient for each type of exposure and the dosimeters were of the calcium fluoride type with a dysprosium impurity. Additional dosimeters were placed over the thyroid, mastoid, cheek, and eyelid in each patient. Exposures for the men were between 75 and 90 kv. and 14 or 15 ma. with a slightly lower range for the women. The readings from the calibrated dosimeters were converted to millirad values.

The total dose administered at some sites in the periapical and bitewing examination is between 10 and 20 times the total dose administered to that site by the panoramic and bitewing examination. The average total exposure is about 5 times greater with the periapical bitewing examination. Complete tables are given showing the variation in various sites. The least reduction in dose with the panoramic examination occurs in the region of the mastoid processes.

Although occasionally additional films are necessary after each type of survey examination, the significant decrease in dose, from approximately 15,000 mrads with the periapical bitewing examination to 3,000 mrads with the panoramic bitewing examination, is well established.—*E. Frederick Lang, M.D.*

Whaley, K., Blair, S., Low, P. S., Chisholm, D. M., Dick, W. C., and Buchanan, W. W. Sialographic abnormalities in Sjögren's syndrome, rheumatoid arthritis, and other arthritides and connective tissue diseases: a clinical and radiological investigation using hydrostatic sialography. *Clin. Radiol.*, Oct., 1972, *23*, 474–482. (From: Centre for Rheumatic Diseases and University Department of Medicine, Royal Infirmary, Glasgow; Department of Oral Medicine and the Department of Radiology, Western Infirmary, Glasgow, Scotland.)

Sjögren's syndrome is a chronic, benign disorder affecting the lacrimal and salivary glands, and results in dryness of the eyes, or keratoconjunctivitis sicca, and dryness of the mouth, or xerostomia.

Sjögren's syndrome was considered a rare disease, but recent experience in a number of centers has indicated that it is relatively common.

Sialography by a hydrostatic technique was performed on 102 patients with Sjögren's syndrome, 123 patients with rheumatoid arthritis, 17 patients with various connective tissue diseases, 81 patients with miscellaneous forms of arthritis and 74 control subjects.

Inter- and intra-observer error in the interpretation of sialographic abnormalities was low and could be completely excluded by using a simple template when reading the sialograms.

In the authors' present study, 60 of the 102 patients (58.8 per cent) with Sjögren's syndrome had sialographic abnormalities; 18 patients had punctate; 14 globular; and 15 cavitary sialectasis. Atrophy of the parotid gland was present in 16 patients and dilatation of the main duct occurred in 22 patients.

Minor sialographic abnormalities were noted in the other clinical groups.

Hydrostatic sialography has been a safe and efficient method of examining salivary glands of patients with Sjögren's syndrome and avoids the danger of gland rupture that may complicate hand injection methods.—*John H. Harris, M.D.*

Neck and Chest

Tsai, Shih H., Anderson, W. Robert, Strickland, Martha B., and Pliego, Mario. Bronchopulmonary dysplasia associated with oxygen therapy in infants with respiratory distress syndrome. *Radiology*, Oct., 1972, *105*, 107–112. (Address: Shih H. Tsai, M.D., Department of Radiology, Hennepin County General Hospital, Fifth and Portland South, Minneapolis, Minn. 55415.)

Bronchopulmonary dysplasia is a complication developing in infants with the respiratory distress syndrome, who were treated with prolonged high concentration oxygen therapy under intermittent positive pressure breathing.

This study includes 47 infants of both sexes, and all but 3 were premature at birth. All had increasing tachypnea, sternal and subcostal retraction, expiratory grunting, cyanosis on breathing room air, and a roentgenographic pattern of diffuse reticulogranularity or opacity with an air bronchogram. The concentration of oxygen given depended on the clinical response and was frequently above 80 per cent. Survival ranged from 3 hours to 23 days with no correlation to birth weight.

Two phases of pulmonary abnormalities were noted: an acute exudative reaction, and, in infants who survived the longest, a fibroproliferative reaction was predominant.

The acute reaction occurred in infants receiving more than 20 hours of oxygen therapy. Proliferative lesions became apparent after 22 hours of oxygen therapy and increased with infant survival and duration of therapy.

After 100 hours of oxygen therapy the lungs of many infants disclosed interstitial fibrosis and focal areas of emphysematous alveoli alternating with coalescent alveoli.

Initial roentgenograms were typical of hyaline membrane disease. Increased severity of the disease was seen after 1 to 24 hours of oxygen therapy. Evidence of bronchopulmonary dysplasia usually was not apparent until 25 to 50 hours of oxygen therapy had been given. An early feature was the development of vacuole-like air spaces in the opacified lung field which evolved into cystic air spaces interspersed with diffuse coarsely granular and/or confluent densities which gradually cleared to form strings and strands. The cardiac size was normal in all cases.

The consequence of prolonged high oxygen concentration therapy in infants with respiratory distress syndrome is discussed. The study was limited to cases with autopsy material; none of the subjects had survived beyond 23 days. However, many infants do survive with roentgenographic improvement, but components of interstitial fibrosis and emphysema may be irreversible.—*M. Sedlmeir, M.D.*

Berkmen, Yahya M. Bronchial obstruction in unresolved pneumonia and its differentiation from bronchogenic carcinoma. *Radiology*, Nov., 1972, *105*, 309–313. (From: Department of Radiology, New York Medical College—Metropolitan Hospital Center, New York, N. Y.)

Pneumonia which has not cleared after 3 weeks is called unresolved pneumonia. This is an alarming sign and immediate diagnostic procedures should be carried out to rule out central bronchogenic carcinoma, benign bronchial lesions and endobronchial metastases. As a general rule, long standing inflammatory processes do not obstruct the bronchi and may be considered a reliable sign in ruling out central bronchial carcinoma. The author has encountered several cases of unresolved pneumonia in which inflammatory obstruction of second- and third-generation bronchi was demonstrated by bronchography.

Of the 4 patients the author studied, 1 had organizing pneumonia, 2 had a pulmonary abscess with slow resolution, and 1 had long-standing pneumonia with an abscess distal to bronchial carcinoma. Obstruction involved 1 bronchus in 1 patient and several bronchi in the other 3. Diagnosis was established by lobectomy, bronchoscopic and cytologic examination and clinical course. Bronchoscopy was performed in all patients.

The roentgenographic findings were as follows: Bronchial obstruction is typically found at the edge of the inflammatory process in unresolved pneumonia and always occurs some distance from the origin of the involved bronchus. The occluded end is smooth and regular; the concavity, when present, is toward the hilus. A sharp central projection is sometime seen extending from this end. This projection may vary in length. Occlusion may be gradual, with smooth, symmetric tapering.

Bronchial obstructions from bronchogenic carcinoma are quite different. The meniscus sign in bronchogenic carcinoma is concave away from the hilus rather than concave toward the hilus as in inflammatory occlusion. In bronchogenic carcinoma occlusion of a bronchus may occur very near or at the origin of the bronchus. The occlusion from bronchogenic carcinoma is asymmetric, irregular and rat-tail in appearance.

The pathogenesis is explained as follows: Bronchial mucosal reddening and inflammatory swelling are often reported by pathologists and observed by bronchoscopists. It is possible that the mucosa of the brochus swells until it obliterates the lumen. If long

segments are involved it will be tapered and if a short segment is involved it will be concave.

The importance of an early and correct diagnosis of bronchogenic carcinoma cannot be overemphasized. All diagnostic methods, including plain chest film roentgenography, tomography, bronchoscopy, and cytology have great merit as well as limitations. However, bronchography offers the best results in patients with centrally located tumors; bronchographic diagnosis of peripheral bronchial or alveolar-cell carcinoma, pulmonary lymphoma, and metastatic lesions is less rewarding.

Patients with bronchogenic carcinoma frequently present clinically and roentgenographically with unresolved pneumonia or pulmonary abscess which does not respond to regular medical treatment. For this reason, "unresolved pneumonia" should always be taken very seriously. The absence of occlusion, distortion, or displacement of the bronchi is a reliable sign that the pneumonia is of nontumoral origin. On the other hand, bronchogenic carcinoma shows partial or total occlusion of the bronchi in about 95 per cent of patients, so that this technique constitutes the best diagnostic method in such cases. It should be noted that bronchial obstruction may also occur in nontumoral conditions such as tuberculosis, sarcoidosis, and silicosis whose bronchographic features cannot always be differentiated from those of occlusion caused by carcinoma. By recognizing the inflammatory nature of bronchial obstruction, a benign lesion will not be labeled malignant, and the elimination of occlusion due to inflammatory changes as a diagnosis will direct attention to other bronchi where carcinoma may be found.—*W. O. Havens, M.D.*

Schiaffini, Angel, and Yerga, Manuel. Broncografía: eliminación del medio de contraste. (Bronchography: elimination of the contrast medium.) *Prensa méd. argent.*, May, 1972, *59*, 584–587. (From: Hospital "Francisco Javier Muñiz," Cátedra de Tisiologia, Buenos Aires, Argentina.)

The authors evaluated the efficiency of Na 274 (which has a lytic effect on bronchial secretions) in helping in the elimination of a barium sulphate-cellulose solution from the bronchial tree following bronchography.

Forty patients were subjected to bronchography. Following the examination 20 patients were given Na 274 parenterally (every 12 hours until 16 mg. was administered). The other 20 patients served as a control group.

It was found that Na 274 was of significant help in accelerating the elimination of the contrast medium. —*Julian B. Alvarez, M.D.*

Maillard, J. N., Huguier, M., Conte-Marti, J., and Lortat-Jacob, J. L. Pronostic éloigné de la résection pour cancer de l'oesophage. (Long range prognosis following resection of carcinoma of the esophagus.) *Presse méd.*, Nov., 1972, *1*, 2737–2741. (Address: J. N. Maillard, Hôpital Louis-Mourier, rue Youri Gagarine, F 92700-Colombes, France.)

The authors believe that surgical treatment of esophageal carcinoma has been at a standstill during the past 20 years.

In an effort to determine the long range prognosis they reviewed the records of 349 patients with carcinoma of the esophagus which was surgically resected. Of these 19 were females. Excluded from this study are the cases of immediate postoperative death.

There was no significant difference in the survival rate between the males and females during the first 3 years. Survival was slightly higher in the female in the 3–5 year period.

For the purpose of determining the tumor site the esophagus is divided into thirds. Cancer of the esophagus whose superior border is above the level of the aortic arch is considered to be a cancer of the upper third of the esophagus. A cancer with its superior border below the root of the lung is considered to be in the lower third. A cancer between the root of the lung and the superior border of the aorta is considered to be in the middle third of the esophagus.

The study is based on a review of the records, roentgenologic and operative findings with a 5 year follow-up.

The lesions varied in size between 1 and 10 cm. in length. Long term survival did not seem to depend on the size, extent, duration or histology of the lesion. However, the prognosis was poorest when regional lymph nodes were involved and when invasion extended through the esophageal wall to the lung, pericardium, and the aorta; also, when distant metastases occurred. In the absence of involvement of the regional lymph nodes or invasion of adjacent structures, lesions of the middle and lower third did not differ in their long range survival rate and had the best prognosis. They were readily amenable to surgical resection. Lesions of the upper third of the esophagus had a poor prognosis, short range survival rate, and the highest postoperative mortality.

Of the 349 patients whose esophageal cancer was surgically removed, the survival rate was 43.9 per cent after 1 year, 16.4 per cent after 3 years, and 9 per cent after 5 years.

In cancer of the middle third of the esophagus the results were better with resection and immediate esophagogastric anastomosis than with total esophagostomy with or without secondary esophagoplasty. —*William H. Shehadi, M.D.*

Abdomen

Wayne, Eli R., and Burrington, John D. Extrinsic duodenal obstruction in children.

Surg., Gynec. & Obst., Jan., 1973, *136*, 87–91. (From: Department of Surgery, The Children's Hospital, Denver, and the Division of Pediatric Surgery, the University of Colorado Medical Center, Denver, Colo.)

Sixty-four children with extrinsic compression of the duodenum were seen at the Colorado General Hospital and The Children's Hospital, Denver, between 1952 and 1971. Seventy per cent were males. The patients were divided into 2 groups.

Group A (39 patients) had congenital peritoneal bands with or without associated malrotation of the duodenum and colon. This group presented early in life with a mean age at operation of 31 days. All but 1 was operated on during the first year of life. For those with an associated midgut volvulus, the mean age at operation was 6 days, the oldest patient being 2 weeks old. Associated midgut volvulus can occur synchronously or the obstructing duodenal bands may bring the patient to surgery before the volvulus obstructs the superior mesenteric vessels. Four types of congenital peritoneal bands are described. Type 1 was always associated with malrotation of the colon and cecum. The bands extended from the cecum across the descending duodenum to the right paravertebral gutter. Type 2 bands run from an abnormally high and medial hepatic flexure across the descending portion of the duodenum to the right paravertebral gutter. Thirty-one of the 39 patients in Group A had either Type 1 or 2 bands. Type 3 bands represented hypertrophy of a normally placed hepatoduodenal ligament. There is no associated malrotation. Symptoms are generally less severe. Type 4 bands always occur with an incompletely rotated duodenum associated with a normally positioned colon. Characteristically the distal part of the transverse duodenum is obstructed by bands that bind the duodenum posteriorly to the paravertebral fascia.

All patients in this group require complete lysis of the bands with mobilization of the involved duodenal segment. Those with Type 4 will also require mobilization of the second, third, and fourth portions of the duodenum and repositioning of the entire duodenum and small intestine into the right paravertebral gutter. An associated midgut volvulus must be reduced and the entire colon placed in the left side of the abdomen. Fixation procedures are unnecessary and add the risk of perforation.

Group B consisted of all other causes of extrinsic duodenal obstruction. This group generally presented later in life with the average age at operation being 9 years with a range of 1 day to 16 years. Four lesions are discussed: superior mesenteric artery syndrome; intramural hematoma; annular pancreas; and duplication of the duodenum. Although the literature is unclear as to whether obstruction of the duodenum by the superior mesenteric artery is a true disease entity, the authors suggest that these patients are best treated with mobilization of the entire duodenum and repositioning of the duodenum and several feet of proximal jejunum into the right paravertebral gutter. Intramural hematomas present 1 to 2 days after abdominal trauma. They may resolve spontaneously in 10 to 14 days. The patients with an annular pancreas all presented at less than 2 weeks of age. Simple duodenoduodenostomy is the procedure of choice. Duplication of the duodenum generally arises in the first or second duodenum. The duplicated segment often does not communicate with the duodenal lumen, although the septum between the duodenum and the duplication may be quite thin. The duplication causes obstruction by accumulated secretions compressing the adjacent normal duodenum. Simple lysis of the septum is the procedure of choice, although a bypass procedure may be necessary.—*Frederick P. Stitik, M.D.*

Doutre, L.-P., Traissac, F.-J., Delorme, G., Perissat, J., Paccalin, J., and Diard, F. Cholangiographie trans-parieto-hépatique par voie extra-péritonéale: confrontations radio-chirurgicales. (Extraperitoneal transhepatic cholangiography; radio-surgical comparisons.) *Presse méd.*, Sept., 1972, *1*, 2231–2234. (From: Services des Cliniques chirurgicale, thérapeutique et radiologique, Hôpital Saint-André, Bordeaux, France.)

The fasting patient is premedicated and placed in the prone position on the examining table. Following local anesthesia of the skin, a needle with a teflon catheter is inserted at the 10th intercostal space at a point 4 fingerbreadths to the right of the midline, to a depth of 10–12 cm. A grating sensation is felt when the needle enters the liver parenchyma.

The needle is then removed and the teflon catheter remains. This is slowly withdrawn until bile begins to flow. If under tension, the bile is allowed to flow until the pressure falls; then a water soluble contrast medium is injected under television-fluoroscopic control. Films are exposed at different stages of the examination in multiple projections, as may seem indicated. The contrast medium remains within the bile ducts and a delayed roentgenogram at 6 hours is obtained giving additional information about the condition and appearance of the bile ducts.

The use of the teflon catheter precludes injury to the parenchyma or blood vessels during respiration. The posterior extraperitoneal approach avoids peritoneal complications due to leakage of bile or blood. The necessity of immediate surgical intervention at the conclusion of the examination is eliminated and a 6 hour delayed follow-up roentgenologic examination is possible.

The examination is contraindicated in liver infections, cholangitis, and blood dyscrasias.

Caution should be exercised in the long hyposthenic patient as well as in cases of kyphoscoliosis

where the anatomic landmarks and peritoneal reflections are altered.

During 1970–71 the authors performed this examination on 34 patients. However, during this same period they operated on 71 other patients with jaundice on whom this examination was not performed.—*William H. Shehadi, M.D.*

Debray, Ch., Leymarios, J., and Hernandez, C. L'artériographie sélective après repas gras dans la parenchymographie pancréatique et grêlique et dans l'exploration des veines splénique, mésentérique supérieure, et porte. (Selective celiac arteriography after a fat meal in pancreatic and small bowel parenchymography and in exploration of the splenic, superior mesenteric, and portal veins.) *Arch. franç. des malad. de l'appar. digest.*, Sept., 1972, *61*, 549–554. (From: Clinique des Maladies de l'Appareil Digestif, Hôpital Bichar, Paris, France.)

Selective celiac arteriography after a fat meal is a valuable procedure in studies of the pancreatic and small intestinal parenchyma and in opacification of the splenic, superior mesenteric, and portal veins.

Marked vasodilatation of the abdominal organs occurs during the digestive period. This vasodilatation is especially pronounced after the ingestion of a fat meal. The lymphatic and venous channels are likewise affected and the abdominal organs become congested.

The authors make use of this phase of vasodilatation to improve the results of the image in selective celiac arteriography.

Twenty-eight adult patients with gastroenterologic problems—abdominal pain, unexplained gastrointestinal hemorrhage, portal hypertension—were examined by this method.

The patient, fasting since the evening before, eats a fat meal, which consists of 50 grams of butter on a small piece of bread, or a protein-fat meal consisting of 60 grams of butter, 20 grams of sugar, 20 grams of protein extract, and 2 grams of coffee extract. Angiography is performed between 1 and 2½ hours after ingestion of the fat meal. Premedication shortly before the examination consists of intramuscular injection of 50 mg. phenergan and 200 mg. meprobromate.

A radiopaque catheter is used with 3 mm. exterior diameter and a 1.3 mm. diameter of the lumen. Depending on the caliber of the celiac trunk, 40–80 ml. of contrast material is injected followed by an equal volume of normal saline at 1–1.2 kg. pressure delivering 5–12 ml. per second.

The examination was well tolerated. There was no nausea or vomiting either during or after the examination.

A parallel series of 28 patients was examined without fat meal and the results were compared to: (1) pancreatic arterial vascularization; (2) pancreatic parenchymal visualization; and (3) appearance of small intestinal parenchyma and the venous return in the splenic and superior mesenteric veins. The results of studies after fat meal ingestion were notably superior.

This study was conducted on patients free of pancreatic disease. A further study should be conducted to determine the extent and significance of variations or absence of pancreatic parenchymal visualization. The procedure is simple and innocuous. The authors plan to pursue their studies to explore its diagnostic value in abnormal conditions.—*William H. Shehadi, M.D.*

Genitourinary System

Joffre, F., Carcy, J. B., Putois, J., Manelfe, C., and Giron, J. Obstructions calicielles par compression infundibulaire vasculaire (syndrome de Fraley). (Obstruction of calyces by vascular compression of the infundibulum [Fraley's syndrome].) *J. de radiol., d'électrol. et de méd. nucléaire*, June–July, 1972, *53*, 485–492. (From: Service Central d'Electroradiologie, C.H.U. Purpan, F.31, Toulouse, France.)

Clinico-roentgenologic correlation has revealed the presence of Fraley's syndrome in 6 of the authors' patients.

In each, nonradiating costovertebral angle pain has been associated with vascular compression of an infundibulum draining an upper pole calyx.

On urography there is a linear defect across the foot of the calyx, which on vascular study is identified as artery or vein. It is the intermittent, and later permanent, dilatation of the calyx proximally which is associated with pain. Later, one observes, as in 3 of this series, irreversible segmental interstitial nephritis.

Compression urograms confirm the nondisappearance of the filling defect. Roentgenograms in various positions are obtained to see if the imprint disappears. Ciné (or tape) recording during urography is indispensable to evaluate the disturbed contractions and poor emptying of the calyx. Progressively, one may see intense and frequent contractions, ineffectual contractions, and absence of contractions.

Tomograms are helpful to search for renal parenchymal atrophy, and arteriography makes such evaluation more precise.

Ptosis of the kidney may play an etiologic role. Pain often is reported worse after prolonged standing; 3 of the present patients had recently lost considerable weight.

Three of the authors' patients underwent surgery and were cured of their syndrome.

When segmental interstitial atrophy has occurred, an upper pole partial nephrectomy may be required. Otherwise, the more conservative choice between

infundibuloplasty or infundibulopyelostomy may be curative.

In the presence of intense pain, or progression which might lead to chronic atrophy, surgery should be considered, and the radiologist's evaluation is important.—*Alan E. Oestreich, M.D.*

Obrez, Ivo, and Abrams, Herbert L. Temporary occlusion of the renal artery: effects and significance. *Radiology*, Sept., 1972, *104*, 545–556. (Address: Herbert L. Abrams, M.D., Department of Radiology, Harvard Medical School, 25 Shattuck Street, Boston, Mass. 02115.)

A number of experimental and clinical studies of the collateral circulation produced by stenosis or occlusion of the renal artery have been undertaken. In this article the authors have studied the effects of varying periods of renal artery obstruction in dogs and its effect on renal function. Control renal arteriograms were first obtained on each animal. Occlusion was then achieved by introducing a Kifa gray catheter with preformed tip into the renal arterial lumen or by inflating the balloon of a modified Rashkind balloon catheter with curved tip. Catheterization was performed *via* the femoral or left carotid artery. The authors also describe 2 case studies of patients whose renal arteries were inadvertently obstructed during renal arteriography.

The pathways of renal collateral circulation were significantly different in each experimental animal. The second, third and fourth lumbar arteries, superior and inferior capsular arteries, phrenicoabdominal artery, and periureteral vessels were the most common sources of collateral circulation. The collateral pathways used in renal ischemia depend not only upon anatomic variations, but also the site and extent of renal artery occlusion. The morphologic and functional characteristics of renal angiography during temporary occlusion of the renal artery are similar to the findings seen in hemorrhagic hypotension. Changes in the distribution of intrarenal blood flow were associated with cortical ischemia and abnormal accumulation of contrast material in the intercortical and medullary zones. In this study the findings suggest that the redistribution of intrarenal blood flow during temporary occlusion of the renal artery is associated not only with diversion of blood from the renal cortex by preglomerular vasoconstriction, but also with rapid renal vein visualization. In 1 dog, who had 2 renal arteries in which only the caudal artery was temporarily occluded, although contrast material had been injected simultaneously into both arteries, there was evidence of profound damage only in the segment supplied by the occluded artery.

In renal injury due to the contrast agent, there is no distinct correlation between the dose and concentration and the extent of damage. However, the authors feel that the contrast agent is more damaging when the circulation is impaired, probably because the "contact time" with the vessel wall is prolonged. In this study, when the lumen of the renal artery was mechanically occluded, there was angiographic visualization of the renal venous system to the level of the subcortical arcades.

There are significant individual variations in the sources and pathways of the renal collateral circulation after acute renal arterial occlusion. The more distal the occlusion from the origin of the renal artery, the more chance there is for collaterals to originate from the aorta or the proximal part of the renal artery. Unintentional occlusion of the renal artery during selective catheterization and injection of contrast material into the occluded artery may result in irreversible damage to the renal parenchyma.

The authors recommend that catheters with end holes, pressure monitoring, control of back-flow at regular intervals and controlled test injections of contrast media may prevent unintentional occlusion of the renal artery.—*E. J. Schoolar, M.D.*

Sanders, Roger C., Textor, John H., Jr., and Bowerman, Jack W. Bladder intramural gas following transurethral prostatectomy. *Brit. J. Radiol.*, Dec., 1972, *45*, 902–904. (From: Department of Radiology, Johns Hopkins Hospital, Baltimore, Md.; Department of Urology, Virginia Commonwealth University; and Institute of Orthopaedics, London, England.)

Gas in the wall of the urinary bladder occurs in the presence of cystitis, particularly if the patient is a diabetic, with an *Escherichia coli* infection, and gas is seen in the urinary bladder after trauma. The authors encountered gas in the bladder wall shown on a film study of the abdomen a few hours after transurethral prostatectomy in which inadvertent perforation of the gallbladder occurred.

Subsequently 14 uncomplicated uninfected patients were examined 1 hour after transurethral resection of the prostate and an additional 6 were examined 18 hours after the operation. In the former group intramural bladder gas was shown in 2, and in the latter, in 1. In all 3 in which intramural air was observed, a considerable amount of prostatic tissue had been removed and it is possible that the prostatic capsule was breached. No other likely basis for the presence of the gas was demonstrated.

The authors feel that the presence of the gas is the result of gas formed by the increase in temperature when the cutting edge of the instrument is used.

The presence of gas in the bladder wall does not indicate poor operative technique, particularly when adequate transurethral resection has been carried out. The presence of intramural air without other evidence of abnormality is thus not of pathologic significance.—*E. Frederick Lang, M.D.*

Nervous System

Djindjian, R., Cophignon, J., Théron, J., Merland, J. J., and Houdard, R. L'embolisation en neuro-radiologie vasculaire: technique et indications à propos de 30 cas. (The embolization in vascular neuroradiology: technique and indications based on 30 cases.) *Presse méd.*, Sept., 1972, *1*, 2153–2158. (Address: Prof. R. Djindjian, Département de Neuro-Radiologie, Hôpital Lariboisière, 2, rue Ambroise-Paré, F 75010, Paris, France.)

Difficulties during surgical management of highly vascular lesions of the nervous system can be diminished or avoided by interventional neuroradiology in appropriate lesions. Surgery at too great a distance from a lesion leaves the possibility of re-establishment of arterial supply, while operation quite close may entail considerable risk. If iatrogenic embolization could suppress the blood supply of only the lesion, it would be preferable. Even without complete obliteration, the surgery can be made easier, and a high risk candidate may receive clinical amelioration.

The Seldinger femoral technique is preferred. This route permits catheterization of terminal branches of the external carotid artery, and seems less traumatic for a large needle puncture than a carotid puncture. Small resorbable sponge-like material is injected as superselectively as possible, to cause local thombi where it lodges.

Spinal cord lesions, especially angiomas and hemangioblastomas, are easily embolized *via* the ostium of the appropriate intercostal artery, if the supply locally is by the posterior spinal route. The procedure is safe for those lesions locally supplied by the anterior radiculomedullary arteries only in the cervical region, where there is multiplicity of supply. If the artery of Adamkiewicz supplies, very tiny particles are used to only partially occlude a mass while avoiding wider ischemia.

The authors believe that the risk of unwanted ischemia is too great to recommend embolization within the internal carotid system, until more selective techniques become possible. On the other hand, the external carotid system can be superselected without risk of cerebral ischemia, and may well benefit from embolization in treatment of A–V fistulas, angiomas, or tumors of high vascularity.—*Alan E. Oestreich, M.D.*

Adams, F. G., and Ward, P. Value of lateral decubitus screening in myelography. *Clin. Radiol.*, Oct., 1972, *23*, 427–433. (From: Department of Radiology, the Royal Infirmary, Sheffield, England.)

By means of 5 cases the authors demonstrate the value of lateral decubitus screening in myelography. The method is of value in the detection of laterally placed lesions, in eliminating flow defects in the dorsal region, and in demonstrating that not all apparent blocks, as shown by conventional myelography, are complete. The method is also of value in examining patients with a severe kyphosis.

Reproductions of 14 roentgenograms are used to demonstrate the value of this procedure.—*John H. Harris, M.D.*

Skeletal System

Bailey, Harry L., Gabriel, Sister Mary, Hodgson, A. R., and Shin, J. S. Tuberculosis of the spine in children: operative findings and results in one hundred consecutive patients treated by removal of the lesion and anterior grafting. *J. Bone & Joint Surg.*, Dec., 1972, *54-A*, 1633–1657. (Address: H. L. Bailey, M.D., 288 Limestone Street, Lexington, Ky. 40508.)

One hundred consecutive children between the ages of 1 and 10 who had proven tuberculosis of the spine underwent excision of all diseased tissue with anterior fusion. Sixty-three of the children were males and 37 females. The average follow-up reported in this paper was 8 years and 2 months. Forty-three of the patients had some degree of paraplegia on admission. Most of the lesions were in the thoracolumbar region with one in the cervical region and 5 patients had double lesions. Seventy-three per cent of the patients had 3 or less vertebral bodies involved. The ninth thoracic vertebra was the most frequently collapsed in the series as a whole. Ninety-six of the patients had some degree of kyphosis, most frequently in the thoracic spine. Thirty-four patients had scoliosis of some degree. When anterior vertebral scalloping was evident on roentgenography, tuberculous abscess involvement was found surgically. All cases showed some degree of narrowing of the intervertebral spaces and sequestra were found in 71 patients. Forty-five patients had tuberculosis at sites other than the spine.

Various surgical approaches were described in the different regions of the spine. Posterior fusion in conjunction with anterior fusion in an unstable spine because of extensive disease was also described in 13 patients. Chemotherapy preoperatively averaged $3\frac{1}{2}$ months with postoperative chemotherapy for 1 year and 10 months. Following completion of the postoperative chemotherapy, isoniazid was often given for 6 months. The average period of postoperative immobilization was $5\frac{1}{2}$ months.

At operation 88 of the patients had abscess and 12 patients had lung penetration. Complications were relatively few with re-operation due to persistent infection required in only 1 patient and fracture of the graft in 12 patients. In the majority of these cases this was attributed by the authors to having left a major portion of the intervertebral disk in the inter-

spaces which were fused. There were 4 patients who had stable nonunions and 10 patients in whom unstable nonunions occurred and over-all follow-up revealed a full working capacity in 94 patients and partial in 6. There were 26 patients in the whole series with nonunion and 19 of these patients had an increase in kyphosis, 4 had loss of height and 3 had nonunion which was subsequently corrected by growth of the vertebral bodies within the fusion mass.

The authors' survey of the literature is reported in their discussion. From the many different series which have been done they conclude that a completely valid comparison of the various treatments of Pott's disease in children by their method of debridement and anterior fusion with other nonoperative methods and treatment by posterior fusion is probably not possible, since the latter methods were employed for the most part prior to the advent of antituberculous therapy. They conclude that the most effective method of dealing with Pott's disease is the technique described in this report.—*Robert P. Andrews, M.D.*

GRIECO, MICHAEL H. *Pseudomonas* arthritis and osteomyelitis. *J. Bone & Joint Surg.*, Dec., 1972, *54-A*, 1693–1704. (From: Allergy and Infectious Disease Section, Department of Medicine, St. Luke's Hospital Center, New York, N. Y.)

Pseudomonas arthritis and osteomyelitis have not been common occurrences, but in this article 5 cases at a single hospital over 18 months are reported and 4 of these cases were considered to represent hospital acquired infection. The 5 cases ranged in age from 17 to 74 years with underlying disease such as arteriosclerotic heart disease, chronic pyelonephritis and viral hepatitis present as prior debilitating considerations. In all patients the *Pseudomonas* osteomyelitis appeared to develop secondary to a contiguous focus of infection: in the tibia, knee, hip, lumbar spine, and sternum. In 4 patients infection developed following bone trauma.

The roentgenographic findings were characteristic of osteomyelitis and included osteolysis, periosteal reaction and osteoblastic activity.

Treatment resulted in apparent cure in 4 patients and 1 probable treatment failure was lost to follow-up.

Although about half of all osteomyelitides are associated with a contiguous focus of infection, all of the patients infected with *Pseudomonas aeruginosa* developed in this manner. In all the patients the presence of fever was related to the duration of the disease and the most frequent symptom was pain in the area of infection.

Although control of infection was achieved with antibiotics, large doses of antibiotics, in particular carbenicillin and gentamycin, seemed to be most effective and with combined use possibly are synergistic. Saucerization was required in 3 of the patients who responded to treatment and closed irrigation with antibiotics was included in the therapeutic program in 3 of the patients.—*Robert P. Andrews, M.D.*

GATTEREAU, ANTOINE, DAVIGNON, JEAN, LANGELIER, MICHEL, and LÉVESQUE, HENRI PAUL. An improved radiological method for the evaluation of Achilles tendon xanthomatosis. *J. Canad. M. A.*, Jan., 1973, *108*, 39–42. (Address: Dr. Antoine Gattereau, Clinical Research Institute of Montreal, 110 Pine Avenue West, Montreal 130, Quebec, Canada.)

Xanthomatosis has long been recognized as the most common and one of the most readily detectable signs of hyperlipidemia. The presence and increase or decrease in size of the xanthomas have been used in evaluating treatment of hypercholesterolemia. Soft tissue roentgenograms have been used for detection and measurement of xanthomas.

The authors describe a standardized method for measuring the thickness of the Achilles tendon which is reproducible and simple to carry out. The frequency of xanthomas in the Achilles tendon and the unsuspected diffuse xanthomatosis in this tendon give these measurements clinical significance.

A lateral roentgenogram is made of each ankle using mammographic technique. This permits easy measurement of the anteroposterior diameter of the Achilles tendon, as outlined by retrotibial fat from before, and subcutaneous fat from behind, at a standardized distance of 8 cm. above the lowest point of the tuberosity of the calcaneus. The normal anteroposterior diameter for males is 6.52 mm. and for females it is 5.38 mm. Repeated measurements in normals are accurate to within 0.5 mm. In hyperlipidemic males of Type II, according to the criteria of Fredrickson *et al.*, the measurement was 9.48 and for females it was 12.05 mm.

The authors suggest that the upper limit of normal for the anteroposterior diameter of the Achilles tendon is 6.9 mm. for males and 5.9 mm. for females. The correlation coefficient for Achilles tendon thickness and plasma cholesterol concentration is 0.854 for females and 0.632 for males.—*E. Frederick Lang, M.D.*

GENERAL

GROS, CH., QUENNEVILLE, Y., and HUMMEL, Y. Diaphanologie mammaire. (Diaphanology of the breast.) *J. de radiol., d'électrol. et de méd. nucléaire*, April, 1972, *53*, 297–306. (Address: Pr. Ch. Gros, Service Central de Radiologie, C.H.U., F.67-Strasbourg, France.)

Since sophisticated transilluminators, with a water cooled powerful source, have become available, their use for breast diagnosis (diaphanology) can again be

considered. Each breast is viewed visually and photographically in semidarkness.

The patterns of normal breasts are: (a) clear and homogeneous, from the uniform adipose breasts of obese or old women; (b) opaque, from the fibrocystic breasts of pregnant or young women; and (c) heterogeneous, in cases of intermediate structure.

Pathologic lesions or their increased blood supply may often be identified. Color examples are shown. In the specific entity of hemorrhagic fluid collections after trauma, diaphanology can reveal a lesion which cannot be discovered by the usual other diagnostic modalities. Cysts distended with fluid are hard to palpate. However, if the liquid does not distend the walls, they are soft. If these soft cysts are filled with hemorrhagic or clear liquid, diaphanology may be required for recognition.

The technique is a painless, bloodless modality which in certain instances complements the other methods of investigation of the breast.—*Alan E. Oestreich, M.D.*

Winter, Thomas Q., and Pearson, Kent D. Systemic sporothrixosis. *Radiology*, Sept., 1972, *104*, 579–583. (Address: Thomas Q. Winter, M.D., Department of Radiology, University of California School of Medicine, San Francisco, Calif.)

Sporotrichosis is a rare, chronic, fungal infection caused by *Sporotrichum schenckii*, and for the most part produces localized ulcerating cutaneous lesions. In rare instances, the disease may spread deeper than the subcutaneous tissue and involve the skeletal system, the lung, and other viscera. In such cases the disease is referred to as systemic sporotrichosis.

The authors reviewed 5 such cases at the National Institutes of Health in Bethesda, Md. and present the roentgenographic appearances seen in these cases.

The findings in these cases, and in reviews by other authors, indicate a high percentage of bone and joint involvement, with the knee, wrist and hand, ankle, and elbow being the most frequently involved areas. The bone and joint involvement is usually found together. Articular involvement is typically characterized by loss of the joint space, joint effusions, irregularity of the articular margins and surrounding soft tissue swelling. Adjacent bone destruction may be a prominent feature. Osteoporosis is not seen often and may help in differentiating sporotrichosis from tuberculous arthritis. Calcifications within the joint may be seen and occur from periarticular bone fragmentation. Periarticular erosions also may occur and indicate a chronic synovitis. Involvement of the small joints of the hands and feet helps in differentiating this entity from other types of infectious arthritis, and the extreme chronicity of the infection, which may extend over several years, also helps exclude most other infections. Skeletal sporotrichosis must be differentiated from tuberculosis, blastomycosis and other fungal infections, osteomyelitis, bacterial arthritis, and destructive rheumatoid arthritis.

Lung involvement, manifested by cavitation, fibronodular infiltrates, pleural effusions, and hilar lymphadenopathy may have an appearance identical to other chronic fungal infections and may co-exist with pulmonary tuberculosis and/or sarcoidosis.

The diagnosis of sporotrichosis is generally made by culturing the *Sporotrichum schenckii* organism, but can also be demonstrated histopathologically. The current treatment of choice for this systemic disease consists of the use of amphotericin B, administered systemically or by direct intraarticular injection.—*Donald N. Dysart, M.D.*

RADIATION THERAPY

Herlitzka, Alfred J., Badruddoja, Mohammed, and Dube, Volker E. Clinical and pathologic features of Burkitt's lymphoma. *Surg., Gynec. & Obst.*, Jan., 1973, *136*, 81–86. (From: Departments of Surgery and Pathology, St. Joseph Mercy Hospital, Mason City, Iowa.)

Burkitt in 1958 described a highly malignant lymphoma which had a marked predilection for the jaw and abdominal viscera of African children. This disease has received widespread attention because of its potential curability by chemotherapy, and marked geographical distribution being confined to malaria-infested equatorial areas. A herpes-like virus has been demonstrated in cell lines derived from this tumor, leading many to consider this condition as the prototype for viral induced neoplasia in man.

Ten cases occurring in Iowa and Wisconsin are reported. The mean age at the time of diagnosis was 7 years, 2 months. The youngest patient was 3 years old and the oldest was 14 years old. There were 8 males and 2 females. Eight had presenting symptoms referable to the gastrointestinal tract. Three of these patients had intussusception with severe lower abdominal pain, rebound tenderness and distention. The other 5 presented with generalized symptoms including bloating, nausea, anorexia and diarrhea. Of these last 5, 4 had palpable masses. The fifth had ascites. Two patients presented initially with head and neck symptoms. One had a congested nasal passage and an enlarged tonsil. The other had a mass in the neck. Delay of diagnosis was between 1 day and 4 weeks.

Seven patients underwent intravenous urography. This was normal in 3, 2 had ureteral obstruction and hydronephrosis, 2 had distortion of the collecting systems suggesting intrarenal tumor. Three patients had pedal lymphangiograms which were normal despite retroperitoneal tumor. Barium enema examination demonstrated an irregular constricting tumor mass in 1 patient.

All specimens presented a similar histologic picture

characterized by a monotonous, uniform overgrowth of tumor cells.

The mean survival in the 8 patients who died was 5.4 months. Complete surgical removal of the mass was not accomplished in any of the patients. Cyclophosphamide (cytoxan) alone or in combination with other antimetabolites was given in all patients. Three patients showed no response to cyclophosphamide. The other 5 had remissions prolonging life up to 13 months. All 5 children with initial remissions developed a tumor at sites different from the original, usually in the central nervous system or bone marrow. Five patients received radiotherapy. In 2 where it was directed at the primary tumor, both patients survived. In the other 3 it was given as a last resort and had no beneficial effect.

Several articles report that Burkitt's tumor is multifocal.

From their experience and review of the literature, the authors suggest 2 treatment guidelines: (1) radical surgical procedures should not be attempted; and (2) residual tumor should be given a trial of radiotherapy in conjunction with cyclophosphamide.—*Frederick P. Stitik, M.D.*

Wang, C. C. Management and prognosis of squamous-cell carcinoma of the tonsillar region. *Radiology*, Sept., 1972, *104*, 667–671. (Address: Department of Radiation Medicine, Massachusetts General Hospital, Boston, Mass. 02114.)

The tonsillar region includes the anterior faucial pillar, the retromolar trigone and the tonsillar fossa. Squamous cell carcinoma arising from these sites is relatively common, and, in the head-and-neck category, it is second in frequency to carcinoma of the larynx.

This paper reports 262 patients, who were treated for carcinoma of the tonsillar region at the Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary from 1957 to June, 1968, inclusive. All patients had histologic confirmation, were treated with radical radiation therapy, and were followed at least 3 years. The TNM system was used to stage all cases.

Of these 262 patients, 107 had carcinoma of the anterior faucial pillar and retromolar trigone, and 155 had carcinoma in the tonsillar fossa. They are divided into these 2 groups, because the patterns of spread from each is so distinct. The incidence and character of the metastatic spread, response to radiotherapy, and prognosis are presented for each group, as well as a description of the radiotherapeutic approach, dose, and subsequent complications.

It is concluded that lesions arising in either anatomic site are radioresponsive and irradiation should be the initial treatment. Early lesions are easily controlled (over half of patients treated were disease free for more than 3 years). Patients with larger lesions do not do as well (less than 20 per cent). In patients with metastatic lymph nodes from carcinoma of the tonsillar fossa, radiation therapy alone may afford complete control (unlike metastatic lymph nodes from lesions arising in the anterior faucial pillar and retromolar trigone, as well as other squamous cell carcinomas of the head and neck, where neck surgery is required). The principal failure of radiation therapy is its inability to sterilize advanced primary disease. In these cases, surgical removal of the postirradiated primary site should be considered (especially in those cases where the lesions are in the anterior faucial pillar and retromolar trigone). Therefore, close cooperation between the radiotherapist and the surgeon is highly desirable.—*Paul M. Kroening, M.D.*

Cox, James D., Gingerelli, Frank, Ream, Norman W., and Maier, John G. Total pulmonary irradiation for metastases from testicular carcinoma. *Radiology*, Oct., 1972, *105*, 163–167. (Address: James D. Cox, Chief, Radiation Therapy Service, Division of Radiation Therapy, Georgetown University Hospital, 3800 Reservoir Road, N.W., Washington, D. C. 20007.)

Treatment with cytotoxic drugs is the usual therapy in patients with pulmonary metastases from testicular carcinoma, found either at the time of presentation, or following surgery and irradiation. However, the combination of total pulmonary irradiation and chemotherapy, although successful in children with Wilms' tumor, has not been utilized in adults with metastatic carcinoma to lung, because these tumors are felt to be less radioresponsive, and thus, the intensity of irradiation necessary for results might lead to unacceptable pulmonary complications.

This paper reports the results obtained over a 4 year period in a small group of patients selected for total pulmonary irradiation at Walter Reed General Hospital in attempts to control metastases from testicular carcinoma.

Both lungs were entirely irradiated in 11 such patients. In 6 of these, chemotherapy alone had been unsuccessful. Actinomycin D was combined with irradiation in 8 patients. Midplane supervoltage doses up to 2,100 rads in 3 weeks were well tolerated. All evidence of pulmonary metastases disappeared in 6 patients. In 3 others, reduction in metastatic size was marked, but brief. All 4 previously untreated patients who received irradiation and concomitant actinomycin D had complete responses, with 2 remaining free of pulmonary disease for prolonged periods. One of the 4 is alive with no evidence of disease 3 years after irradiation. This patient is receiving maintenance chemotherapy.

The authors stress the prudence of sequential irradiation of the 2 lungs rather than simultaneous

treatment when such treatment is combined with chemotherapeutic agents.

Although they felt it impossible to determine to what extent actinomycin D and irradiation were additive in their patients, a complete response occurred in all their patients who were previously untreated for their pulmonary disease. They conclude that such therapy may prove advantageous, particularly when maintenance chemotherapy is utilized, and suggest that such possibilities are worthy of further investigation.—*D. E. Marley, Jr., M.D.*

Manale, Bernard L., and Brower, Thomas D. The significance of bacterial flora in carcinoma in chronic osteomyelitis. *Surg., Gynec. & Obst.*, Jan., 1973, *136*, 63–64. (From: Department of Surgery, University of Kentucky Medical Center, Lexington, Ky.)

Ten patients with chronic osteomyelitis and subsequent malignant degeneration are reported. Nine had frank cancer, the other had pseudoepitheliomatous hyperplasia. The average duration of symptoms of osteomyelitis was 50.5 years. Six presumably had hematogeneous osteomyelitis by history. The wound was cultured prior to operation while the patient was not being treated with antibiotics. Only 1 of these patients grew *Staphylococcus aureus* (the patient with pseudoepitheliomatous hyperplasia). *Staphylococcus aureus* is commonly cultured in patients with chronic osteomyelitis despite the duration of the infection and repeated courses of antibiotics. Gram-positive cocci, however, were seen on gram stain in nearly all cases.

The authors surmise that the pathogens were indeed present, but were unable to reproduce rapidly and, therefore, became indolent because of local conditions produced by the cancer. Possibilities include changes in oxygen tension, tissue pH, or competition for a substrate. In the absence of the usual clinical manifestations of malignant degeneration such as pain, foul odor, increased or bloody discharge, fungating mass or pathologic fracture, a change in bacterial flora may be a clue to occult malignant degeneration.—*Frederick P. Stitik, M.D.*

Feldman, Frieda, and Norman, David. Intra- and extraosseous malignant histiocytoma (malignant fibrous xanthoma). *Radiology*, Sept., 1972, *104*, 497–508. (From: Department of Radiology, College of Physicians and Surgeons, Columbia—Presbyterian Medical Center, New York, N. Y.)

The authors studied 20 cases of malignant histiocytoma with skeletal involvement and discuss the pathologic, clinical, and roentgenographic features of the disease. They reviewed the history and histopathology of the many forms of the disease and the confusing array of names which have been attached to its variations.

Those lesions emphasized in this article involved bone, either primarily or by direct extension from adjacent soft tissue. Histologically, the tumors generally could be categorized by the predominant cell pattern: (a) malignant fibrous xanthoma type; (b) malignant fibrous histiocytoma type; (c) malignant histiocytoma type; and (d) malignant giant cell tumor type. Most tumors contained some or all 4 subtypes and no prognostic significance could be related to the predominance of a particular cellular pattern. The difficulty in predicting malignant potential of a lesion based upon its cytologic features is emphasized. Size, local aggressiveness, and mitotic activity are not always definitive criteria for distinguishing benign and malignant lesions.

In reviewing the clinical features of the disease, the authors include a total of 80 cases, of which the 20 with skeletal involvement are a portion. Clinically, the most common presenting complaint was a mild and intermittently painful mass which had been present for a year or less. Of the 20 with bone involvement, 14 demonstrated distant osseous metastases during the course of the disease.

Roentgenographically, both primary and metastatic osseous lesions were mostly purely lytic with moth-eaten and geographic patterns of destruction. The lesions usually had ragged, poorly-defined margins and showed no evidence of internal trabeculation. Periosteal reaction was seen in 5 instances. A total of 14 pathologic fractures in 10 patients was observed.

Differential diagnostic possibilities of the bone lesions are discussed. A history of a soft tissue tumor of an extremity or the chest wall, which histologically looks like a fibrous or xanthomatous lesion, may be a helpful clue to the diagnosis. Even in apparently benign lesions, prognosis must be guarded.—*John M. Stoebner, M.D.*

Harrington, Kevin D., Johnston, James O., Turner, Roderick H., and Green, David L. The use of methylmethacrylate as an adjunct in the internal fixation of malignant neoplastic fractures. *J. Bone & Joint Surg.*, Dec., 1972, *54-A*, 1665–1676. (Address: K. D. Harrington, M.D., 3899 Sacramento Street, San Francisco, Calif. 94118.)

Methylmethacrylate in the management of pathologic fracture is suggested as a possibility because of difficulty commonly encountered when trying to stabilize such fractures and to permit healing and firm moulding. In the cavity left following curettage of the tumor, moulding can occur once the methacrylate has polymerized re-establishing skeletal continuity. The use of this technique in 30 patients is reported with femoral involvement in 26 of the cases, the tibia in 3, the humerus in 2 and the acetabulum

in 2. Sixteen patients had metastatic breast tumors, and other sites represented included 4 with reticulum cell sarcoma, 3 with cancer of the bowel and 2 with cancer of the kidney. Twenty-eight patients regained the ability to walk and 2 remained bed-ridden but enjoyed relative freedom from pain following completion of the surgery. In only 1 patient was reoperation necessitated by failure of internal fixation. Nine patients had a prosthetic replacement of the femoral head and neck.

After tumor curettage the medullary canal of the bone was enlarged sufficiently to allow the methacrylate to cover the entire prosthesis stem. The technique of curettage permitted maximum contact between the methacrylate and the cortical bone, and the union was accomplished with either the slow-curing Cranioplast or the more commonly used surgical simplex P under hypothermic conditions. Examples of several of the cases are presented including intertrochanteric and subtrochanteric fractures of the femur.

In their discussion, the authors make the point that the primary benefit of this technique is the rapid return of the incurable patient to an active status with full weight bearing on the extremities permitted as soon as incisional tenderness allows. The average time from operation to commencement of full weight bearing was 7 days and with the void in the bone filled by methacrylate progressive settling of the fracture fragments or angulation at the fracture site did not occur. Since the life expectancy of these patients is short, the use of the technique is justified even though the placement of methacrylate effectively prevents healing of the fracture. In 16 patients who received local irradiation postoperatively, no compromise of the clinical effects sought by surgery was noted and there were no significant changes in tissues which could be attributed to interaction between radiation and the metal or cement.

In the authors' summary, they point out that this method achieves immediate solid fracture immobilization with consequent alleviation of pain, early active joint motion, and early weight bearing. Although true fracture healing probably does not occur, in only 1 patient did fixation failure take place.—*Robert P. Andrews, M.D.*

Adelstein, A. M., and Donovan, J. W. Malignant disease in children whose mothers had chicken pox, mumps, or rubella in pregnancy. *Brit. M. J.*, Dec., 1972, *4*, 629–631. (Address: A. M. Adelstein, M.D., Chief Medical Statistician, Office of Population Censuses and Surveys, London WC2R 1LR, England.)

To test the hypothesis that leukemia may follow virus infection in pregnancy, deaths of children born in 1951 and 1952 after pregnancies in which the mothers suffered virus infections were examined. The virus infections included were chicken pox and mumps at any stage of gestation and rubella in the first 18 weeks. Deaths in the children between the ages of 2 and 19 years were considered, and the total number of mothers with virus infections was 1,006. Of these 270 had chicken pox, 433 had mumps, and 303 had rubella in the first 18 weeks.

From all causes in all groups, 9.09 deaths were expected, and 7 were found. The causes of death among children of mothers with rubella were not remarkable. Both deaths in children from mothers who had suffered from chicken pox were as a result of leukemia, and this is a statistically significant excess. The causes of death in children whose mothers had contracted mumps were noteworthy because of their rarity, one being from Still's disease and the other from Ewing's sarcoma.

These findings are in agreement with conclusions which have been reported by others, that cases of influenza in pregnancy were followed by a greatly increased number of diagnosis of leukemia in the children. Others report leukemia following other virus infections, such as maternal infectious hepatitis, herpes zoster, and lymphoblastoma after rubella.

In these reports of the development of influenza followed by leukemia in the child, the influenza occurred as early as 12 weeks and as late as 36 weeks of gestation. In the case of the 2 mothers reported here, the chicken pox occurred in the twenty-third and the twenty-fifth weeks of pregnancy.—*E. Frederick Lang, M.D.*

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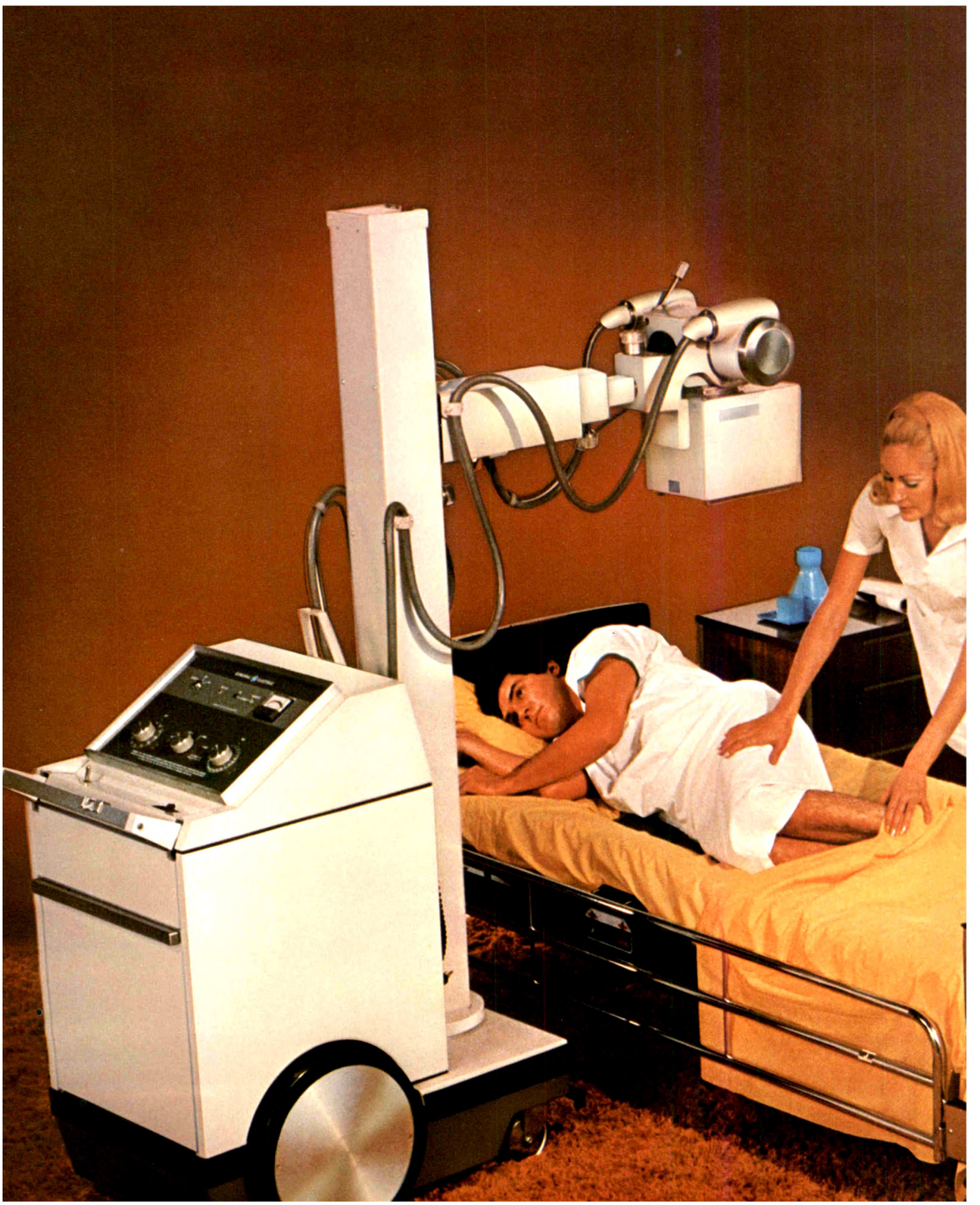
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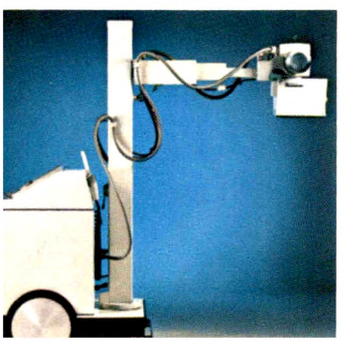
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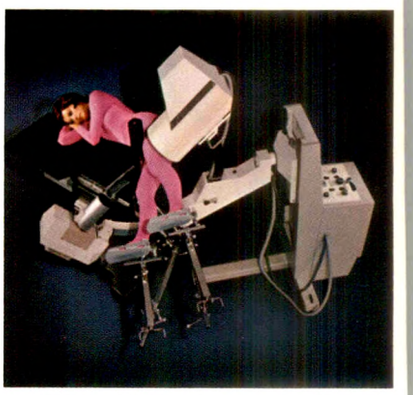
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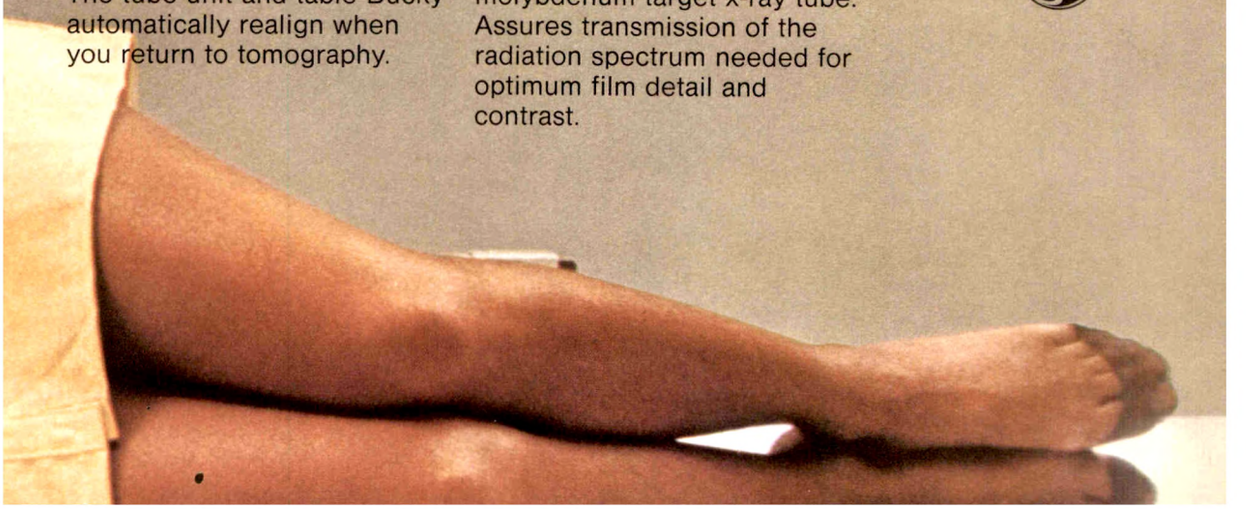
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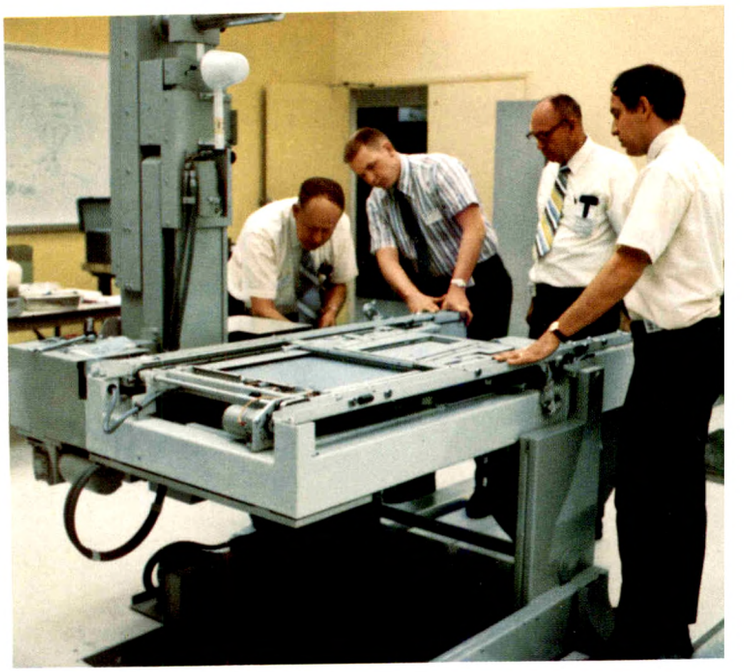


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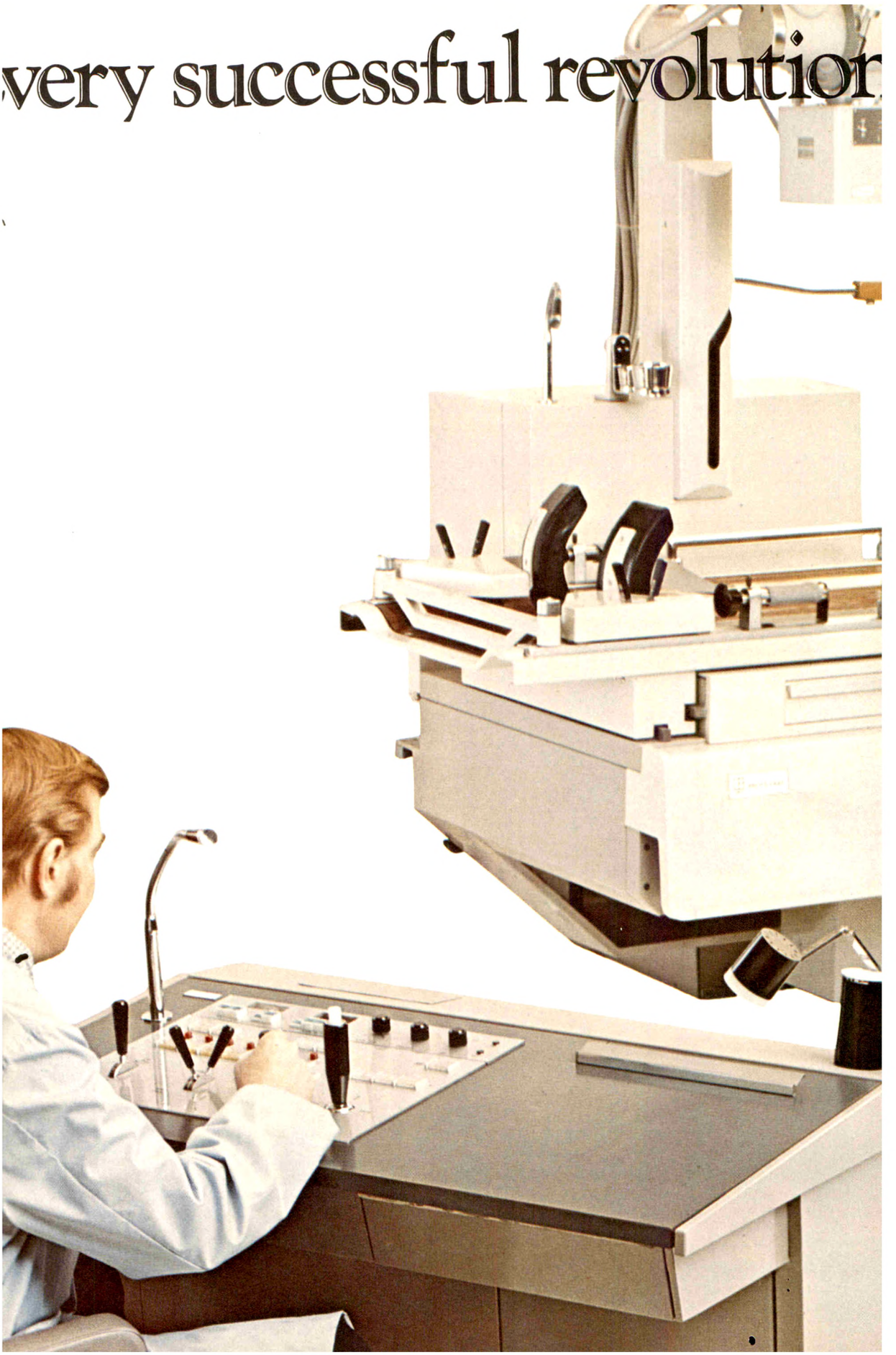
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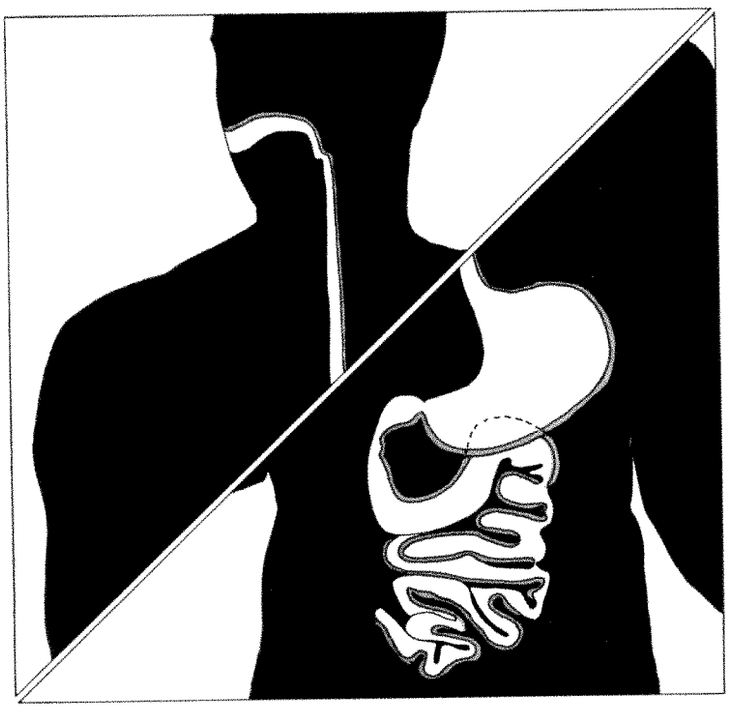
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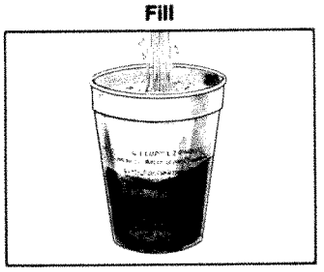
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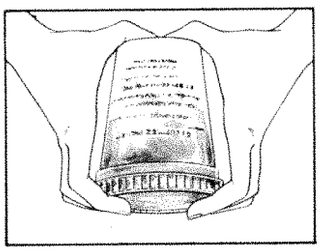
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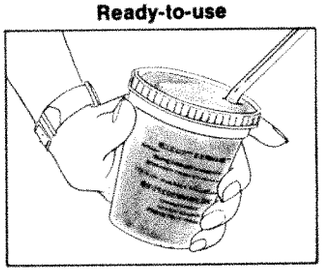
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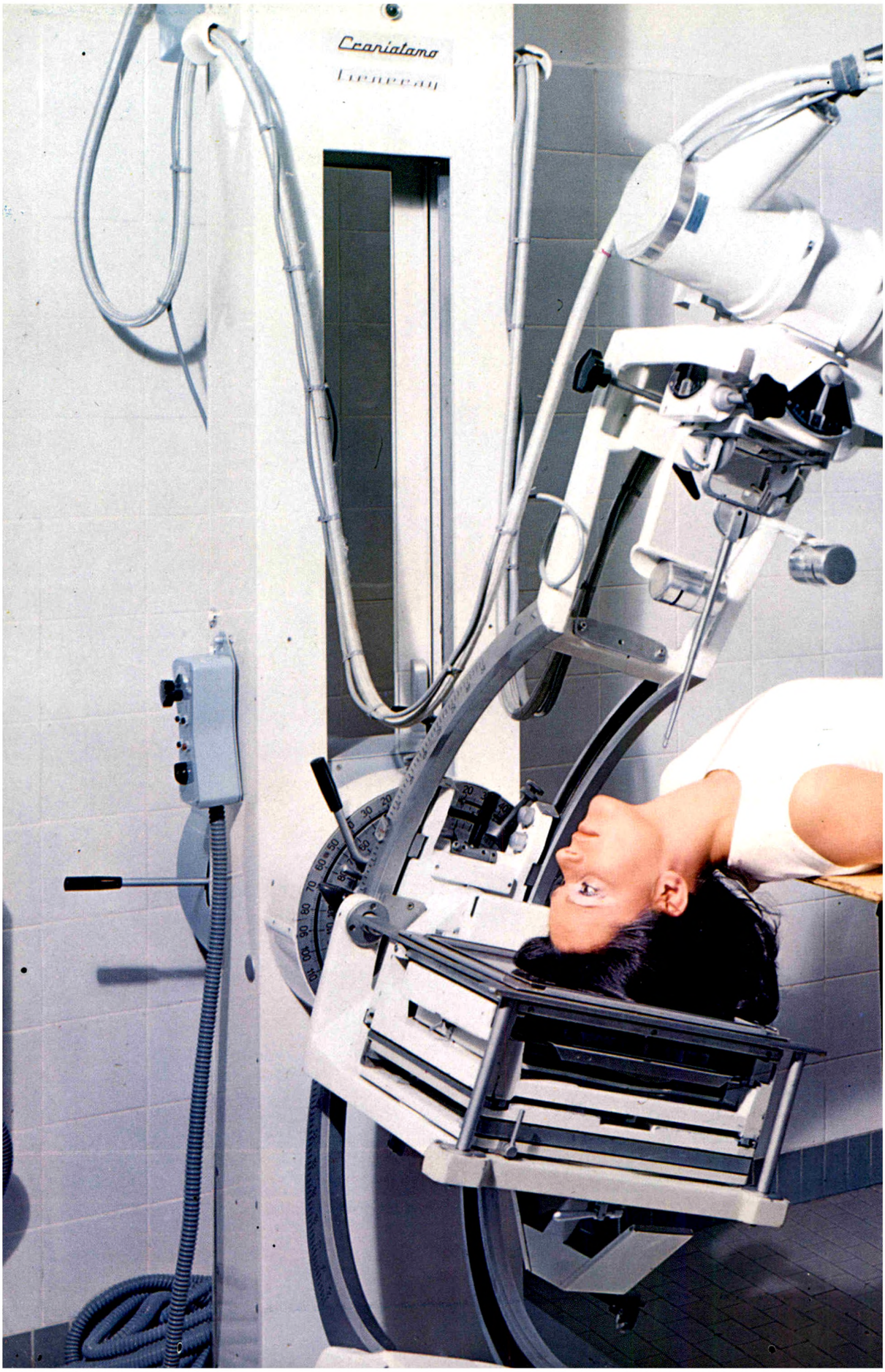
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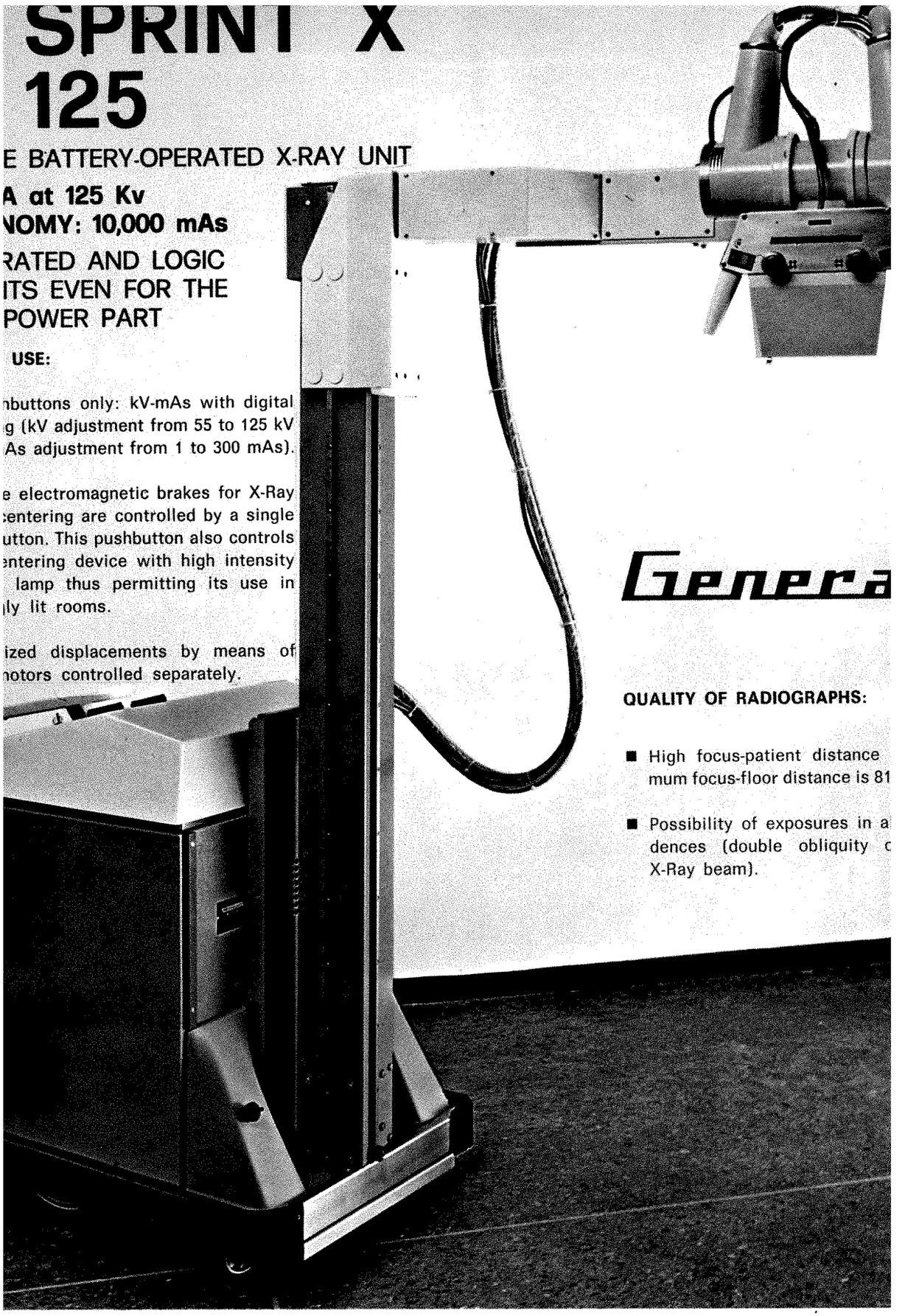
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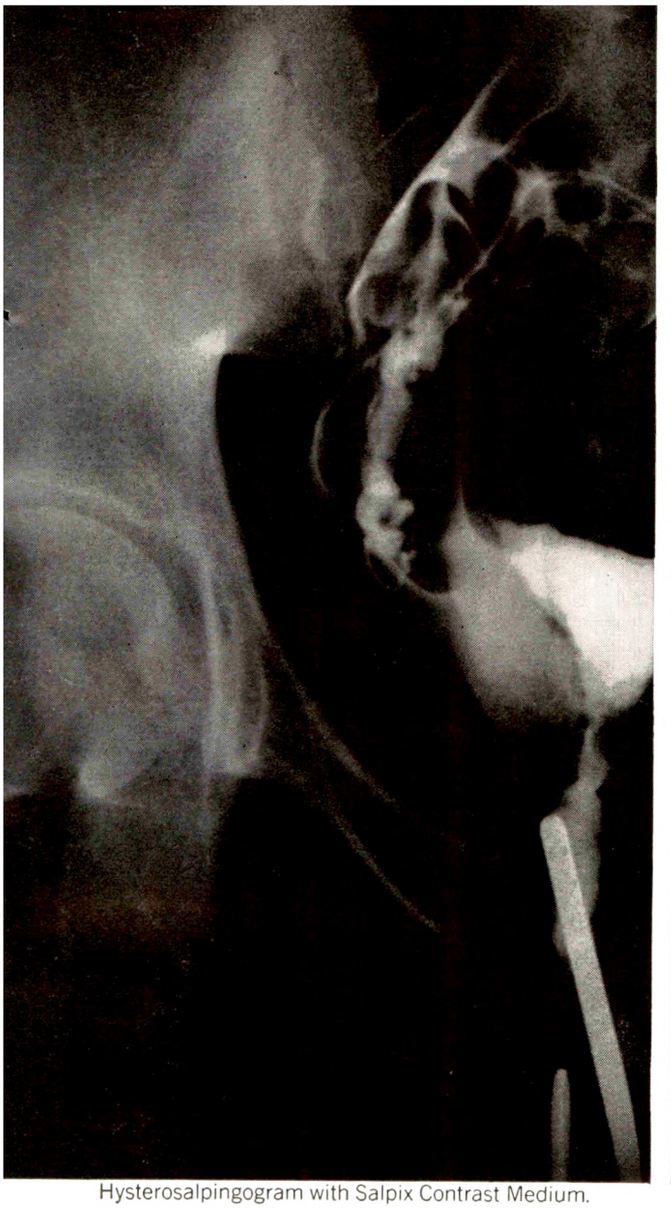
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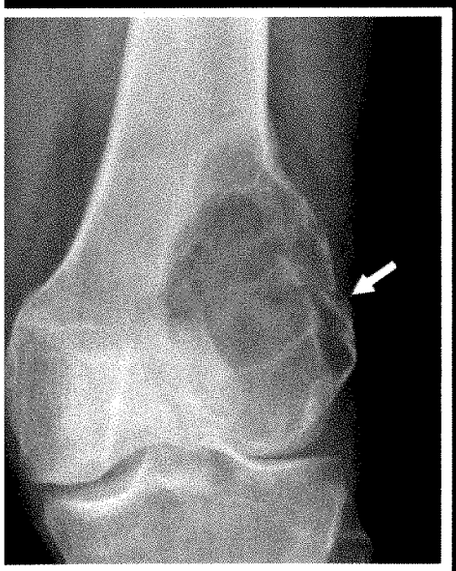
The many faces of Giant-Cell Tumors

"Eccentric! Subarticular! After the epiphysis has fused!" Yet giant-cell tumors do not always do so!

Classical giant-cell tumors of bone are distinctive bone-destroying neoplasms that usually are found in the epiphysis of long bones. More than half occur about the knee, the distal femur being affected more commonly than the proximal tibia. Third in frequency is the distal end of the forearm where the distal radius is especially vulnerable. By far the majority of giant-cell tumors are encountered beyond the age of 19 years; the peak incidence is the third decade of life.

Usually, giant-cell tumors are juxta-articular; rarely do they enter the joint. Eccentrically placed, they destroy bone asymmetrically. Characteristically, the advancing edges of the tumor elicit but little reactive bone formation except where it thins the cortex. Here, the constant attempt of the periosteum to cover the tumor with a shell of new bone gives the tumor its cyst-like character.

Far less common are giant-cell tumors of small bones, particularly those of the hands and feet. Often confused with benign cartilaginous tumors, or ordinary cysts, giant-cell tumors ought always be thought of when destructive bone lesions are found in patients near 19 years of age or the decade thereafter.



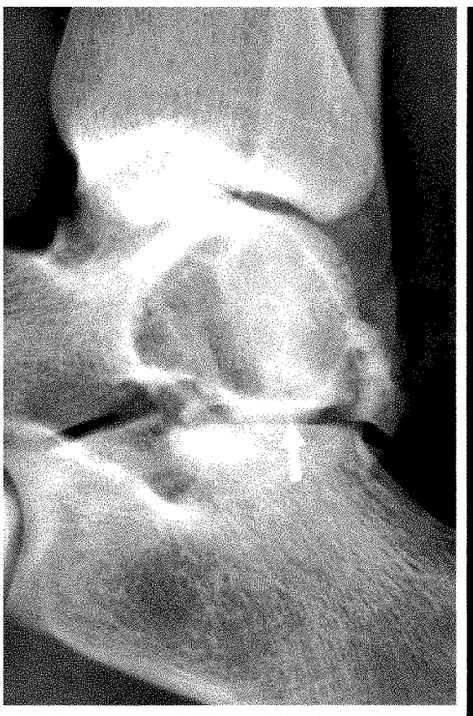
ant-Cell Tumor: Distal Femur. A 22-year-old man complained of pain for three years. Her centric bone lesion extends to the articulat- surface of the femur. Perifocal reactive ne is minimal. The trabeculae seen within cystic lesion are the remnants of destroyed ne and are not the result of (or are not used by) new-bone reaction. Note the patho- ical fracture (arrow).



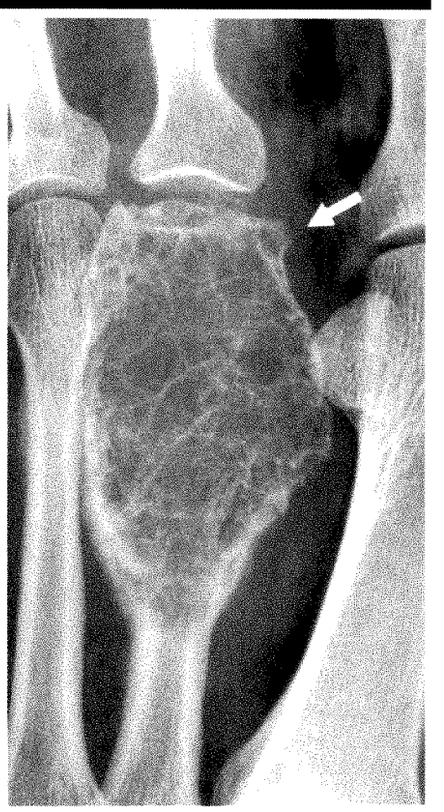


Giant-Cell Tumor: Calcaneus. An 8-year-old girl had ankle pain for four years. This eccentrically placed bone-destroying lesion extends from the epiphyseal plate to within one centimeter of the calcaneocuboid articulation (arrow). A fairly well-defined zone of reactive bone has developed along the medial aspect of the tumor (A) with a barely perceptible layer of cortical bone encapsulating its lateral margin (B). (Anteroposterior projection of the

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marginated, bone-destroying lesion that affects the subtalar joint (arrow). Moderate reactive bone envelops the abnormality. The septa, which are seen with difficulty within the tumor, are all that remain of normal trabeculae.



Giant-Cell Tumor: Metatarsal. A 22-year-old man with a well-demonstrated osteolytic lesion that affects an articular surface. A thin shell-like layer of cortical bone envelops the lesion. Delicate septa mark the remnants of the original trabeculae.



ant-Cell Tumor: Metacarpal. A most unual lesion in the wrong age group (the tient was a 5-year-old boy) and in the ong part of a tubular bone (diaphysis

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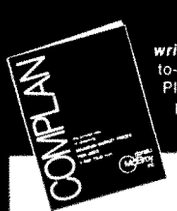
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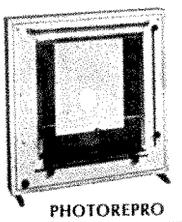
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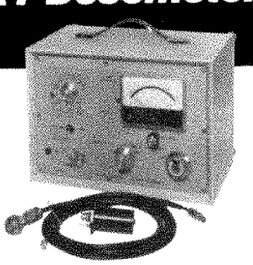
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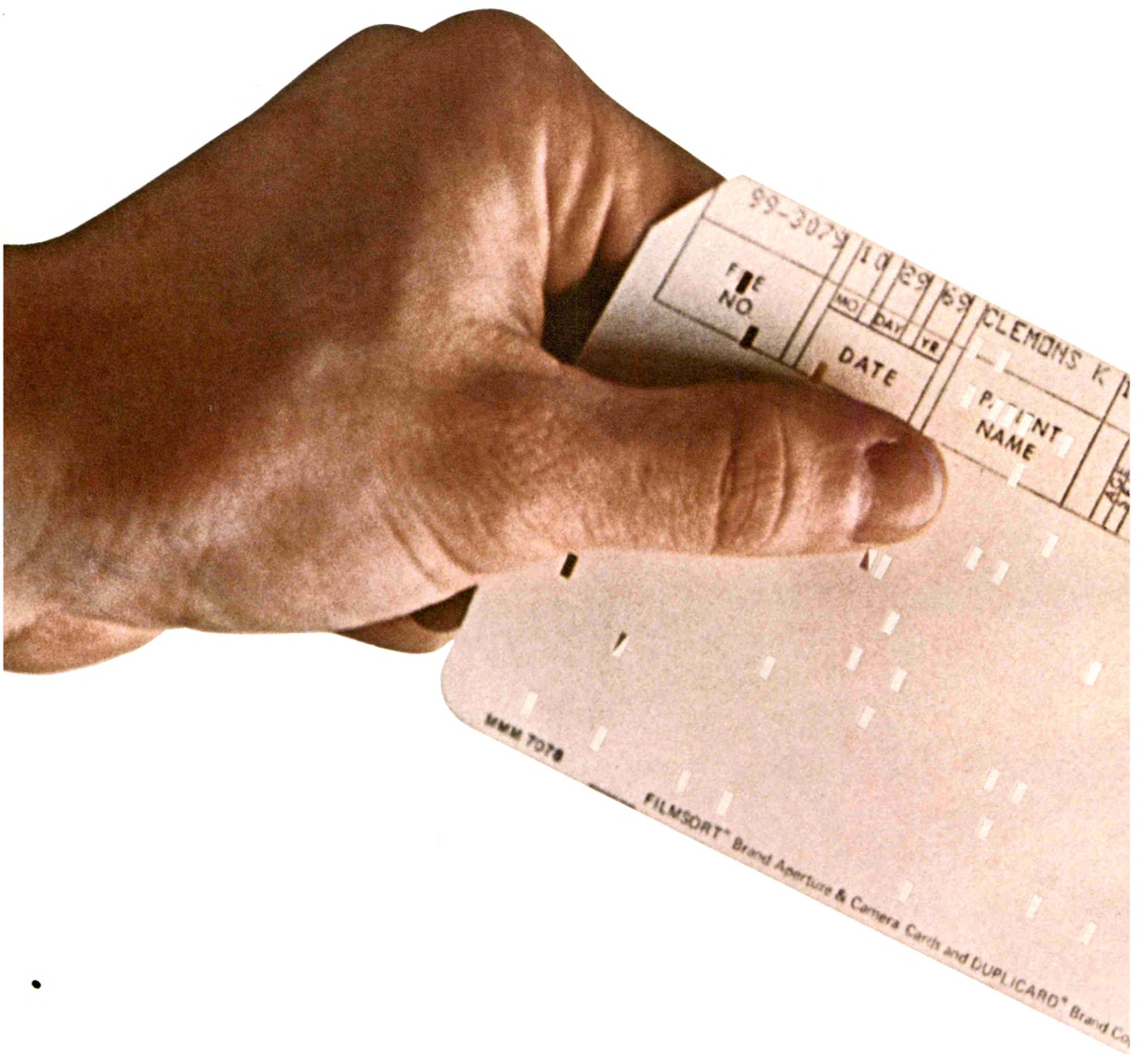
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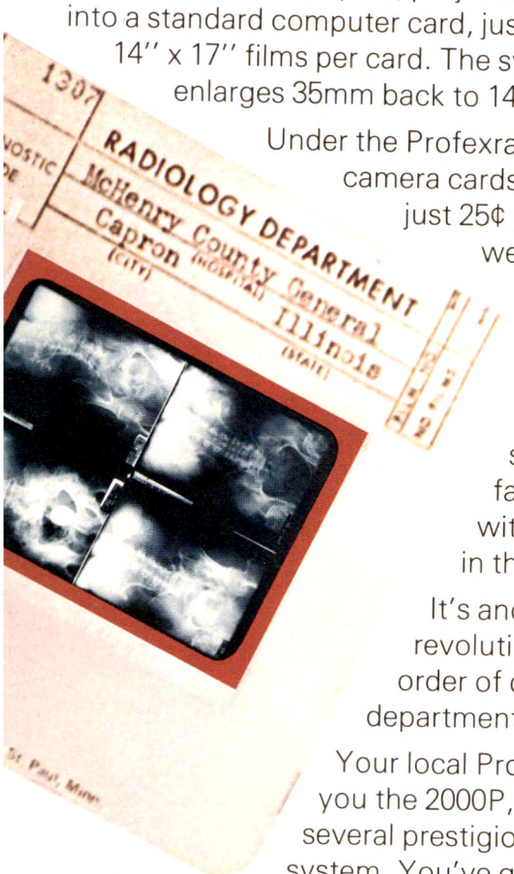
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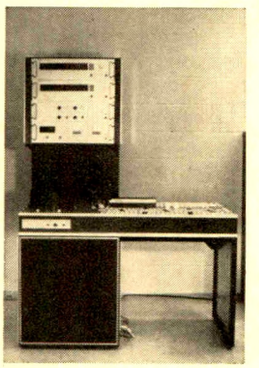
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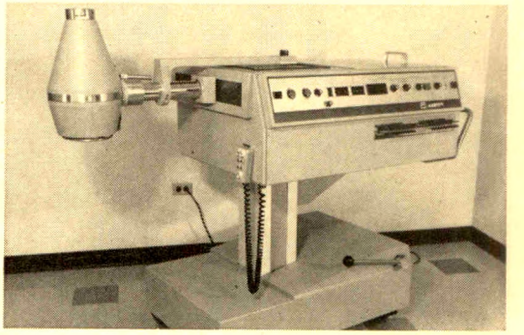
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IN-VIVO

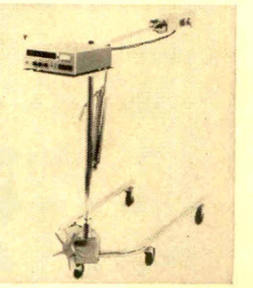
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